

## SEQUENCE LISTING

- <110> Hauptmann, Rudolph Himmler, Adolph Maurer-Fogy, Ingrid Stratowa, Christian
- <120> TNF Receptors, TNF Binding Proteins and DNAs Coding for  $$\operatorname{\textbf{Them}}$$
- <130> 98-385-H
- <140> 09/899,422
- <141> 2001-07-03
- <150> 09/525,998
- <151> 2000-03-15
- <150> 08/383,676
- <151> 1995-02-01
- <150> 08/153,287
- <151> 1993-11-17
- <150> 07/821,750
- <151> 1992-01-02
- <150> 07/511,430
- <151> 1990-04-20
- <160> 97
- <170> PatentIn Ver. 2.0
- <210> 1
- <211> 1368
- <212> DNA
- <213> Homo sapiens
- <220>
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- <222> (1)..(1365)
- <220>
- <221> sig\_peptide
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- <220>
- <221> misc\_feature
- <222> (88)..(120)
- <223> portion of TNF-BP pro protein cleaved by
   extracellular proteases following secretion
- <220>
- <221> misc\_feature
- <222> (606)..(633)
- <223> portion of TNF-BP pro protein cleaved by

## extracellular proteases following secretion

| <400 | )> 1 |   |   |   |   |   |   |   |   |   |   |   |   |                   |   |     |
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| _    |      |   |   |   |   |   | _ | _ | _ | _ |   | - |   | ctc<br>Leu<br>15  | _ | 48  |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | gtc<br>Val        |   | 96  |
|      |      |   | _ |   |   | - | _ |   | - |   | _ |   |   | gga<br>Gly        |   | 144 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | cac<br>His        |   | 192 |
|      |      |   | _ |   |   | _ | _ |   |   | _ |   | _ | _ | acg<br>Thr        | _ | 240 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | cac<br>His<br>95  |   | 288 |
|      |      | _ |   | _ | _ |   |   | - |   |   |   |   |   | cag<br>Gln        |   | 336 |
|      |      |   |   | _ |   |   | - |   | _ |   |   | _ |   | tgc<br>Cys        |   | 384 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | tgc<br>Cys        |   | 432 |
|      | -    | _ |   | _ |   |   |   |   |   |   |   |   |   | cag<br>Gln        |   | 480 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | aga<br>Arg<br>175 |   | 528 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | tgc<br>Cys        |   | 576 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | gac<br>Asp        |   | 624 |
|      |      |   |   |   |   |   |   |   |   |   |   |   |   | tgc<br>Cys        |   | 672 |

|            | 210               |                   |                   |            |            | 215               |                   |                   |            |            | 220               |                   |                   |            |            |      |
|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|-------------------|-------------------|-------------------|------------|------------|------|
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | cgg<br>Arg        |            |            | 720  |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | gaa<br>Glu        |            |            | 768  |
|            |                   |                   | _                 |            |            |                   |                   |                   |            |            |                   |                   | aac<br>Asn<br>270 |            |            | 816  |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | agt<br>Ser        |            |            | 864  |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | ggt<br>Gly        |            |            | 912  |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | tat<br>Tyr        |            |            | 960  |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | atc<br>Ile        |            |            | 1008 |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | agc<br>Ser<br>350 |            |            | 1056 |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | gtg<br>Val        |            |            | 1104 |
| ttg<br>Leu | cgc<br>Arg<br>370 | tgg<br>Trp        | aag<br>Lys        | gaa<br>Glu | ttc<br>Phe | gtg<br>Val<br>375 | cgg<br>Arg        | cgc<br>Arg        | cta<br>Leu | Gly        | ctg<br>Leu<br>380 | agc<br>Ser        | gac<br>Asp        | cac<br>His | gag<br>Glu | 1152 |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | gag<br>Glu        |            |            | 1200 |
|            |                   |                   |                   |            |            |                   |                   |                   |            |            |                   |                   | cgc<br>Arg        |            |            | 1248 |
| acg<br>Thr | ctg<br>Leu        | gag<br>Glu        | ctg<br>Leu<br>420 | ctg<br>Leu | gga<br>Gly | cgc<br>Arg        | gtg<br>Val        | ctc<br>Leu<br>425 | cgc<br>Arg | gac<br>Asp | atg<br>Met        | gac<br>Asp        | ctg<br>Leu<br>430 | ctg<br>Leu | ggc<br>Gly | 1296 |
| tgc<br>Cys | ctg<br>Leu        | gag<br>Glu<br>435 | gac<br>Asp        | atc<br>Ile | gag<br>Glu | gag<br>Glu        | gcg<br>Ala<br>440 | ctt<br>Leu        | tgc<br>Cys | ggc<br>Gly | ccc<br>Pro        | gcc<br>Ala<br>445 | gcc<br>Ala        | ctc<br>Leu | ccg<br>Pro | 1344 |

1368

ccc gcg ccc agt ctt ctc aga tga Pro Ala Pro Ser Leu Leu Arg 450 455

<210> 2

<211> 455

<212> PRT

<213> Homo sapiens

<400> 2

Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu

1 5 10 15

Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro 20 25 30

His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys 35 40 45

Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys 50 55 60

Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 65 70 75 80

Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu 85 90 95

Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val 100 105 110

Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg 115 120 125

Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe 130 135 140

Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu 145 150 155 160

Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu 165 170 175

Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Thr 180 185 190

Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser 195 200 205

Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu 210 215 220

Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys 225 230 235 240

| Ser         | Lys            | Leu        | Tyr        | Ser<br>245 | Ile        | Val        | Cys        | Gly        | Lys<br>250 | Ser        | Thr        | Pro        | Glu        | Lys<br>255 | Glu        |    |
|-------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|----|
| Gly         | Glu            | Leu        | Glu<br>260 | Gly        | Thr        | Thr        | Thr        | Lys<br>265 | Pro        | Leu        | Ala        | Pro        | Asn<br>270 | Pro        | Ser        |    |
| Phe         | Ser            | Pro<br>275 | Thr        | Pro        | Gly        | Phe        | Thr<br>280 | Pro        | Thr        | Leu        | Gly        | Phe<br>285 | Ser        | Pro        | Val        |    |
| Pro         | Ser<br>290     | Ser        | Thr        | Phe        | Thr        | Ser<br>295 | Ser        | Ser        | Thr        | Tyr        | Thr<br>300 | Pro        | Gly        | Asp        | Cys        |    |
| Pro<br>305  | Asn            | Phe        | Ala        | Ala        | Pro<br>310 | Arg        | Arg        | Glu        | Val        | Ala<br>315 | Pro        | Pro        | Tyr        | Gln        | Gly<br>320 |    |
| Ala         | Asp            | Pro        | Ile        | Leu<br>325 | Ala        | Thr        | Ala        | Leu        | Ala<br>330 | Ser        | Asp        | Pro        | Ile        | Pro<br>335 | Asn        |    |
| Pro         | Leu            | Gln        | Lys<br>340 | Trp        | Glu        | Asp        | Ser        | Ala<br>345 | His        | Lys        | Pro        | Gln        | Ser<br>350 | Leu        | Asp        |    |
| Thr         | Asp            | Asp<br>355 | Pro        | Ala        | Thr        | Leu        | Туr<br>360 | Ala        | Val        | Val        | Glu        | Asn<br>365 | Val        | Pro        | Pro        |    |
| Leu         | Arg<br>370     | Trp        | Lys        | Glu        | Phe        | Val<br>375 | Arg        | Arg        | Leu        | Gly        | Leu<br>380 | Ser        | Asp        | His        | Glu        |    |
| Ile<br>385  | Asp            | Arg        | Leu        | Glu        | Leu<br>390 | Gln        | Asn        | Gly        | Arg        | Cys<br>395 | Leu        | Arg        | Glu        | Ala        | Gln<br>400 |    |
| Tyr         | Ser            | Met        | Leu        | Ala<br>405 | Thr        | Trp        | Arg        | Arg        | Arg<br>410 | Thr        | Pro        | Arg        | Arg        | Glu<br>415 | Ala        |    |
| Thr         | Leu            | Glu        | Leu<br>420 | Leu        | Gly        | Arg        | Va1        | Leu<br>425 | Arg        | Asp        | Met        | Asp        | Leu<br>430 | Leu        | Gly        |    |
| Cys         | Leu            | Glu<br>435 | Asp        | Ile        | Glu        | Glu        | Ala<br>440 | Leu        | Cys        | Gly        | Pro        | Ala<br>445 | Ala        | Leu        | Pro        |    |
| Pro         | Ala<br>450     | Pro        | Ser        | Leu        | Leu        | Arg<br>455 |            |            |            |            |            |            |            |            |            |    |
| <212        | L> 48<br>2> DN | ΙA         | sapie      | ens        |            |            |            |            |            |            |            |            |            |            |            |    |
|             | L> CI          |            | (483)      |            |            |            |            |            |            |            |            |            |            |            |            |    |
| <400<br>gat |                | ata        | tat        | aac        | caa        | gga        | aaa        | tat        | atc        | cac        | act        | caa        | aa+        | aat        | tee        | 48 |
|             |                |            |            |            |            |            |            |            |            |            |            |            |            | Asn<br>15  |            |    |

| att tgc<br>Ile Cys                           | Cys Tl | _            | _   |           |           |           |           |     | _         |           |           | _         | _   | 96  |
|--|--------|--------------|-----|-----------|-----------|-----------|-----------|-----|-----------|-----------|-----------|-----------|-----|-----|
| cca ggc                                      |        |              |     |           |           |           |           |     |           | _         |           | _         |     | 144 |
| ttc acc<br>Phe Thr .<br>50                   | -      | _            |     |           |           | _         |           | -   |           | -         | -         |           |     | 192 |
| tgc cga<br>Cys Arg 1<br>65                   |        |              |     |           |           |           |           |     |           |           |           |           |     | 240 |
| cgg gac<br>Arg Asp                           |        |              |     |           |           |           |           |     |           |           |           |           |     | 288 |
| agt gaa<br>Ser Glu                           | Asn Le |              |     |           |           |           |           |     |           |           |           |           |     | 336 |
| acc gtg<br>Thr Val                           |        |              |     |           |           |           |           |     |           |           |           |           |     | 384 |
| cat gca<br>His Ala<br>130                    |        |              |     |           |           |           |           |     |           |           |           |           |     | 432 |
| tgt aag<br>Cys Lys<br>145                    |        |              |     |           |           |           |           |     |           |           |           |           |     | 480 |
| aat<br>Asn                                   |        |              |     |           |           |           |           |     |           |           |           |           |     | 483 |
| <210> 4<br><211> 16<br><212> PR<br><213> Hot | Т      | piens        |     |           |           |           |           |     |           |           |           |           |     |     |
| <400> 4<br>Asp Ser                           | Val C  | ys Pro<br>5  | Gln | Gly       | Lys       | Tyr       | Ile<br>10 | His | Pro       | Gln       | Asn       | Asn<br>15 | Ser |     |
| Ile Cys                                      |        | nr Lys<br>20 | Cys | His       | Lys       | Gly<br>25 | Thr       | Tyr | Leu       | Tyr       | Asn<br>30 | Asp       | Cys |     |
| Pro Gly                                      | Pro G  | ly Gln       | Asp | Thr       | Asp<br>40 | Cys       | Arg       | Glu | Cys       | Glu<br>45 | Ser       | Gly       | Ser |     |
| Phe Thr .                                    | Ala S  | er Glu       | Asn | His<br>55 | Leu       | Arg       | His       | Cys | Leu<br>60 | Ser       | Cys       | Ser       | Lys |     |

| Cys<br>65            | Arg                     | Lys         | Glu        | Met       | Gly<br>70  | Gln        | Val        | Glu        | Ile       | Ser<br>75  | Ser        | Cys        | Thr                   | Val              | Asp<br>80  |     |
|----------------------|-------------------------|-------------|------------|-----------|------------|------------|------------|------------|-----------|------------|------------|------------|-----------------------|------------------|------------|-----|
| Arg                  | Asp                     | Thr         | Val        | Суs<br>85 | Gly        | Cys        | Arg        | Lys        | Asn<br>90 | Gln        | Tyr        | Arg        | His                   | Tyr<br>95        | Trp        |     |
| Ser                  | Glu                     | Asn         | Leu<br>100 | Phe       | Gln        | Cys        | Phe        | Asn<br>105 | Cys       | Ser        | Leu        | Cys        | Leu<br>110            | Asn              | Gly        |     |
| Thr                  | Val                     | His<br>115  | Leu        | Ser       | Cys        | Gln        | Glu<br>120 | Lys        | Gln       | Asn        | Thr        | Val<br>125 | Cys                   | Thr              | Cys        |     |
| His                  | Ala<br>130              | Gly         | Phe        | Phe       | Leu        | Arg<br>135 | Glu        | Asn        | Glu       | Cys        | Val<br>140 | Ser        | Cys                   | Ser              | Asn        |     |
| Cys<br>145           | Lys                     | Lys         | Ser        | Leu       | Glu<br>150 | Суѕ        | Thr        | Lys        | Leu       | Cys<br>155 | Leu        | Pro        | Gln                   | Ile              | Glu<br>160 |     |
| Asn                  |                         |             |            |           |            |            |            |            |           |            |            |            |                       |                  |            |     |
| <212<br><213<br><220 | .> 48<br>!> DN<br>!> Ar | JA<br>rtifi | icial      |           |            |            | rial       | Seg        | len ce    | a. re      | acom!      | oinar      | <b>.</b> <del>t</del> |                  |            |     |
|                      | TI                      |             | sec        |           |            |            | ciai       | sequ       | ience     | e: r€      | ecom       | oinai      | 10                    |                  |            |     |
|                      | > CI                    |             | (486)      | )         |            |            |            |            |           |            |            |            |                       |                  |            |     |
|                      | gat                     |             |            |           |            |            |            |            |           |            |            |            |                       | aat<br>Asn<br>15 |            | 48  |
| _                    |                         | _           | _          |           | _          | _          |            |            |           |            |            | -          |                       | aat<br>Asn       |            | 96  |
|                      |                         |             |            |           |            |            |            |            |           |            |            |            |                       | agc<br>Ser       |            | 144 |
|                      |                         |             |            |           |            |            |            |            |           |            |            |            |                       | tgc<br>Cys       |            | 192 |
|                      |                         |             |            |           |            |            |            |            |           |            |            |            |                       | aca<br>Thr       |            | 240 |
|                      |                         |             |            |           |            |            |            |            |           |            |            |            |                       |                  |            |     |

| gac cgg gac<br>Asp Arg Asp   |   |   |                                  |                                |  |  |                                       |                                |                         |                         |                                | 288 |
|--|---|---|----------------------------------|--------------------------------|--|--|---------------------------------------|--------------------------------|-------------------------|-------------------------|--------------------------------|-----|
| tgg agt gaa<br>Trp Ser Glu   |   |   |                                  |                                |  |  |                                       |                                |                         |                         |                                | 336 |
| ggg acc gtg<br>Gly Thr Val<br>115  |   |   |                                  |                                |  |  |                                       |                                |                         |                         |                                | 384 |
| tgc cat gca<br>Cys His Ala<br>130  |   |   | ı Arg                            |                                |  |  |                                       |                                |                         |                         |                                | 432 |
| aac tgt aag<br>Asn Cys Lys<br>145  | aaa agc<br>Lys Ser                                      | ctg gag<br>Leu Glu<br>150                             | tgc<br>Cys                       | acg<br>Thr                     | aag<br>Lys   | ttg<br>Leu<br>155                            | tgc<br>Cys                            | cta<br>Leu                     | ccc<br>Pro              | cag<br>Gln              | att<br>Ile<br>160              | 480 |
| gag aat<br>Glu Asn   |   |   |                                  |                                |  |  |                                       |                                |                         |                         |                                | 486 |
| <210> 6<br><211> 162<br><212> PRT<br><213> Artif   | icial Sec   | quence  |                                  |                                |  |  |                                       |                                |                         |                         |                                |     |
|  |   |   |                                  |                                |  |  |                                       |                                |                         |                         |                                |     |
| <220><br><223> Descr<br>TNF-B  | iption o  |   | lcial                            | Seqı                           | uence  | e: re  | ecom                                  | oina                           | nt                      |                         |                                |     |
| <223> Descr  | P sequen  | ce  |                                  |                                |  |  |                                       |                                |                         | Asn<br>15               | Asn                            |     |
| <223> Descr<br>TNF-B<br><400> 6<br>Met Asp Ser   | Val Cys<br>5<br>Cys Thr                                 | ce<br>Pro Gli   | n Gly<br>s His                   | Lys                            | Tyr<br>10<br>Gly                                   | Ile<br>Thr                                   | His<br>Tyr                            | Pro<br>Leu                     | Gln                     | 15<br>Asn               |                                |     |
| <223> Descr<br>TNF-B<br><400> 6<br>Met Asp Ser<br>1  | Val Cys<br>5<br>Cys Thr<br>20                           | ce<br>Pro Gli<br>Lys Cys                              | n Gly<br>s His                   | Lys<br>Lys<br>25               | Tyr<br>10<br>Gly                                   | Ile<br>Thr                                   | His<br>Tyr                            | Pro<br>Leu                     | Gln<br>Tyr<br>30        | 15<br>Asn               | Asp                            |     |
| <223> Descr<br>TNF-B<br><400> 6<br>Met Asp Ser<br>1<br>Ser Ile Cys                               | Val Cys<br>5<br>Cys Thr<br>20<br>Pro Gly                | Pro Gli<br>Lys Cy:<br>Gln Asp                         | n Gly His Thr 40                 | Lys<br>Lys<br>25<br>Asp        | Tyr<br>10<br>Gly<br>Cys                            | Ile<br>Thr                                   | His<br>Tyr<br>Glu                     | Pro<br>Leu<br>Cys<br>45        | Gln<br>Tyr<br>30<br>Glu | 15<br>Asn<br>Ser        | Asp<br>Gly                     |     |
| <223> Descr TNF-B  <400> 6 Met Asp Ser 1  Ser Ile Cys  Cys Pro Gly 35  Ser Phe Thr               | Val Cys<br>5<br>Cys Thr<br>20<br>Pro Gly                | Pro Gli<br>Lys Cys<br>Gln Asp<br>Glu Ass<br>5!        | o Gly Thr 40                     | Lys<br>Lys<br>25<br>Asp        | Tyr<br>10<br>Gly<br>Cys                            | Ile<br>Thr<br>Arg                            | His<br>Tyr<br>Glu<br>Cys<br>60        | Pro<br>Leu<br>Cys<br>45<br>Leu | Gln Tyr 30 Glu Ser      | 15<br>Asn<br>Ser<br>Cys | Asp<br>Gly<br>Ser              |     |
| <223> Descr TNF-B <400> 6 Met Asp Ser 1 Ser Ile Cys Cys Pro Gly 35 Ser Phe Thr 50 Lys Cys Arg    | Val Cys 5 Cys Thr 20 Pro Gly Ala Ser Lys Glu            | Pro Gli Lys Cys Gln Asi Glu Asi 55 Met Gly 70         | o Gly Thr 40 His                 | Lys<br>25<br>Asp<br>Leu<br>Val | Tyr<br>10<br>Gly<br>Cys<br>Arg                     | Ile<br>Thr<br>Arg<br>His<br>Ile<br>75        | His<br>Tyr<br>Glu<br>Cys<br>60<br>Ser | Pro Leu Cys 45 Leu Ser         | Gln Tyr 30 Glu Ser Cys  | 15<br>Asn<br>Ser<br>Cys | Asp<br>Gly<br>Ser<br>Val       |     |
| <223> Descr TNF-B <400> 6 Met Asp Ser 1 Ser Ile Cys Cys Pro Gly 35 Ser Phe Thr 50 Lys Cys Arg 65 | Val Cys 5 Cys Thr 20 Pro Gly Ala Ser Lys Glu Thr Val 85 | Pro Gli Lys Cys Gln Asi Glu Asi 5! Met Gli 70 Cys Gli | o Thr<br>40<br>His<br>Gln<br>Cys | Lys<br>25<br>Asp<br>Leu<br>Val | Tyr<br>10<br>Gly<br>Cys<br>Arg<br>Glu<br>Lys<br>90 | Ile<br>Thr<br>Arg<br>His<br>Ile<br>75<br>Asn | His Tyr Glu Cys 60 Ser                | Pro Leu Cys 45 Leu Ser         | Gln Tyr 30 Glu Ser Cys  | 15 Asn Ser Cys Thr      | Asp<br>Gly<br>Ser<br>Val<br>80 |     |

| 130 135 140   |  |
|---|--|
| Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile<br>145 150 155 160  |  |
| Glu Asn   |  |
|   |  |
| <210> 7 <211> 633 <212> DNA <213> Artificial Sequence   |  |
| <220> <223> Description of Artificial Sequence: recombinant TNF-BP sequence   |  |
| <220> <221> CDS <222> (1)(633)  |  |
| <400> 7   |  |
| atg ggc ctc tcc acc gtg cct gac ctg ctg ctg cca ctg gtg ctc ctg 48  Met Gly Leu Ser Thr Val Pro Asp Leu Leu Pro Leu Val Leu Leu  1 5 10 15            |  |
| gag ctg ttg gtg gga ata tac ccc tca ggg gtt att gga ctg gtc cct 96 Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro 20 25 30           |  |
| cac cta ggg gac agg gag aag aga gat agt gtg tgt ccc caa gga aaa 144<br>His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys<br>35 40 45    |  |
| tat atc cac cct caa aat aat tcg att tgc tgt acc aag tgc cac aaa 192 Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys 50 55 60          |  |
| gga acc tac ttg tac aat gac tgt cca ggc ccg ggg cag gat acg gac Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 65 70 75 80           |  |
| tgc agg gag tgt gag agc ggc tcc ttc acc gct tca gaa aac cac ctc 288 Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu 85 90 95          |  |
| aga cac tgc ctc agc tgc tcc aaa tgc cga aag gaa atg ggt cag gtg 336 Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Met Gly Gln Val 100 105 110       |  |
| gag atc tct tct tgc aca gtg gac cgg gac acc gtg tgt ggc tgc agg 384<br>Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg<br>115 120 125 |  |

Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser

| aag aac cag<br>Lys Asn Gln<br>130   |  |  | Trp                            |                                |  |                                       |                            |  |                                |                                |                        | 432 |
|---|--|--|--------------------------------|--------------------------------|--|---------------------------------------|----------------------------|--|--------------------------------|--------------------------------|------------------------|-----|
| aat tgc agc<br>Asn Cys Ser<br>145   |  |  |                                |                                |  |                                       |                            |  |                                |                                |                        | 480 |
| aaa cag aac<br>Lys Gln Asn  |  |  |                                |                                |  |                                       |                            |  |                                |                                |                        | 528 |
| aac gag tgt<br>Asn Glu Cys  | _  |  |                                | -                              | -  |                                       |                            |  |                                |                                |                        | 576 |
| aag ttg tgc<br>Lys Leu Cys<br>195   | Leu Pro  |  |                                |                                |  |                                       |                            |  |                                |                                |                        | 624 |
| ggc acc aca<br>Gly Thr Thr<br>210   |  |  |                                |                                |  |                                       |                            |  |                                |                                |                        | 633 |
| <210> 8<br><211> 211<br><212> PRT<br><213> Artif  | icial Sed  | guence   |                                |                                |  |                                       |                            |  |                                |                                |                        |     |
| ZIJ- MICIL  | TCTAL DC   | Juence   |                                |                                |  |                                       |                            |  |                                |                                |                        |     |
| <220><br><223> Descr  |  | f Artifi   | cial                           | Sequ                           | ience  | e: re                                 | ecomb                      | oinar  | nt                             |                                |                        |     |
| <220><br><223> Descr  | iption o:<br>P sequend   | f Artifi<br>ce   |                                |                                |  |                                       |                            |  |                                | Leu<br>15                      | Leu                    |     |
| <220> <223> Descr TNF-B <400> 8 Met Gly Leu   | iption of<br>P sequend<br>Ser Thr<br>5   | f Artifi<br>ce<br>Val Pro  | Asp                            | Leu                            | Leu<br>10  | Leu                                   | Pro                        | Leu  | Val                            | 15                             |                        |     |
| <220> <223> Descr TNF-B <400> 8 Met Gly Leu 1   | iption of<br>P sequence<br>Ser Thr<br>5<br>Val Gly<br>20                           | f Artifi<br>ce<br>Val Pro<br>Ile Tyr                                   | Asp<br>Pro                     | Leu<br>Ser<br>25               | Leu<br>10<br>Gly                                   | Leu<br>Val                            | Pro<br>Ile                 | Leu<br>Gly                                   | Val<br>Leu<br>30               | 15<br>Val                      | Pro                    |     |
| <220> <223> Descr TNF-B  <400> 8 Met Gly Leu 1 Glu Leu Leu His Leu Gly                                      | iption of<br>P sequence<br>Ser Thr<br>5<br>Val Gly<br>20<br>Asp Arg                | f Artifice  Val Pro  Ile Tyr  Glu Lys                                  | Asp<br>Pro<br>Arg<br>40        | Leu<br>Ser<br>25<br>Asp        | Leu<br>10<br>Gly<br>Ser                            | Leu<br>Val<br>Val                     | Pro<br>Ile<br>Cys          | Leu<br>Gly<br>Pro<br>45                      | Val<br>Leu<br>30<br>Gln        | 15<br>Val<br>Gly               | Pro<br>Lys             |     |
| <220> <223> Descr TNF-B  <400> 8 Met Gly Leu 1  Glu Leu Leu  His Leu Gly 35  Tyr Ile His                    | iption of P sequence  Ser Thr  5  Val Gly 20  Asp Arg                              | f Artifice  Val Pro  Ile Tyr  Glu Lys  Asn Asn 55                      | Asp<br>Pro<br>Arg<br>40<br>Ser | Leu<br>Ser<br>25<br>Asp        | Leu<br>10<br>Gly<br>Ser<br>Cys                     | Leu<br>Val<br>Val<br>Cys              | Pro Ile Cys Thr            | Leu<br>Gly<br>Pro<br>45<br>Lys               | Val<br>Leu<br>30<br>Gln<br>Cys | 15<br>Val<br>Gly<br>His        | Pro<br>Lys<br>Lys      |     |
| <220> <223> Descr TNF-B  <400> 8 Met Gly Leu 1  Glu Leu Leu  His Leu Gly 35  Tyr Ile His 50  Gly Thr Tyr    | iption of P sequence  Ser Thr  5  Val Gly 20  Asp Arg  Pro Gln  Leu Tyr            | f Artifice  Val Pro  Ile Tyr  Glu Lys  Asn Asn 55  Asn Asp 70          | Asp Pro Arg 40 Ser Cys         | Leu<br>Ser<br>25<br>Asp<br>Ile | Leu<br>10<br>Gly<br>Ser<br>Cys                     | Leu<br>Val<br>Val<br>Cys<br>Pro       | Pro Ile Cys Thr 60 Gly     | Leu<br>Gly<br>Pro<br>45<br>Lys<br>Gln        | Val Leu 30 Gln Cys             | 15<br>Val<br>Gly<br>His        | Pro Lys Lys Asp 80     |     |
| <220> <223> Descr TNF-B  <400> 8 Met Gly Leu 1  Glu Leu Leu  His Leu Gly 35  Tyr Ile His 50  Gly Thr Tyr 65 | iption of P sequence  Ser Thr 5  Val Gly 20  Asp Arg  Pro Gln  Leu Tyr  Cys Glu 85 | f Artifice  Val Pro  Ile Tyr  Glu Lys  Asn Asn 55  Asn Asp 70  Ser Gly | Asp Pro Arg 40 Ser Cys         | Leu Ser 25 Asp Ile Pro         | Leu<br>10<br>Gly<br>Ser<br>Cys<br>Gly<br>Thr<br>90 | Leu<br>Val<br>Val<br>Cys<br>Pro<br>75 | Pro Ile Cys Thr 60 Gly Ser | Leu<br>Gly<br>Pro<br>45<br>Lys<br>Gln<br>Glu | Val Leu 30 Gln Cys Asp         | 15<br>Val<br>Gly<br>His<br>Thr | Pro Lys Lys Asp 80 Leu |     |

| 115  |  | 120   | 125  |
|--|--|---|--|
| Lys Asn Gln Ty<br>130  | -  | yr Trp Ser Glu Asn<br>35  | Leu Phe Gln Cys Phe<br>140   |
| Asn Cys Ser Le   | eu Cys Leu As<br>150   | sn Gly Thr Val His  | Leu Ser Cys Gln Glu<br>160   |
| Lys Gln Asn Th   | r Val Cys Th<br>165  | hr Cys His Ala Gly<br>170   | Phe Phe Leu Arg Glu<br>175   |
| Asn Glu Cys Va   |  | er Asn Cys Lys Lys<br>185   | Ser Leu Glu Cys Thr<br>190   |
| Lys Leu Cys Le<br>195  | eu Pro Gln I   | le Glu Asn Val Lys<br>200   | Gly Thr Glu Asp Ser<br>205   |
| Gly Thr Thr<br>210   |  |   |  |
| <210> 9<br><211> 549<br><212> DNA<br><213> Artifici  | al Sequence  |   |  |
| =  |  | ficial Sequence: re   | combinant  |
| TNF-BP s   | equence  |   |  |
| TNF-BP s <220> <221> CDS <222> (1)(54)   |  |   |  |
| <220> <221> CDS <222> (1)(54) <400> 9 atg ctg gtc co   | 9)<br>et cac cta g   |   | aga gat agt gtg tgt 48<br>Arg Asp Ser Val Cys<br>15  |
| <220> <221> CDS <222> (1)(54) <400> 9 atg ctg gtc commet Leu Val Pro 1 ccc caa gga aa Pro Gln Gly Ly   | et cac cta go<br>to His Leu G<br>5   | ly Asp Arg Glu Lys<br>10<br>ac cct caa aat aat  | Arg Asp Ser Val Cys  |
| <220> <221> CDS <222> (1)(54) <400> 9 atg ctg gtc co Met Leu Val Pr 1  ccc caa gga aa Pro Gln Gly Ly aag tgc cac aa  | et cac cta gg to His Leu G 5 ta tat atc ca s Tyr Ile H:  | ly Asp Arg Glu Lys 10  ac cct caa aat aat is Pro Gln Asn Asn 25  ac ttg tac aat gac   | Arg Asp Ser Val Cys 15  tcg att tgc tgt acc 96 Ser Ile Cys Cys Thr   |
| <220> <221> CDS <222> (1)(54) <400> 9 atg ctg gtc co Met Leu Val Pr 1 ccc caa gga aa Pro Gln Gly Ly aag tgc cac aa Lys Cys His Ly 35 cag gat acg ga                                      | et cac cta go to His Leu G  to | ly Asp Arg Glu Lys 10  ac cct caa aat aat is Pro Gln Asn Asn 25  ac ttg tac aat gac yr Leu Tyr Asn Asp 40  ag tgt gag agc ggc   | Arg Asp Ser Val Cys 15  tcg att tgc tgt acc 96 Ser Ile Cys Cys Thr 30  tgt cca ggc ccg ggg 144 Cys Pro Gly Pro Gly   |
| <220> <221> CDS <222> (1)(54) <400> 9 atg ctg gtc co Met Leu Val Pr 1  ccc caa gga aa Pro Gln Gly Ly  aag tgc cac aa Lys Cys His Ly 35  cag gat acg ga Gln Asp Thr As 50  gaa aac cac ct | et cac cta gent of the cac ctac cac cac cac cac cac cac cac ca   | ly Asp Arg Glu Lys 10  ac cct caa aat aat is Pro Gln Asn Asn 25  ac ttg tac aat gac yr Leu Tyr Asn Asp 40  ag tgt gag agc ggc lu Cys Glu Ser Gly 55  gc ctc agc tgc tcc | Arg Asp Ser Val Cys 15  tcg att tgc tgt acc 96 Ser Ile Cys Cys Thr 30  tgt cca ggc ccg ggg 144 Cys Pro Gly Pro Gly 45  tcc ttc acc gct tca 192 Ser Phe Thr Ala Ser |

| 85   |  | 90  | 95   |     |
|--|--|---|--|-----|
| tgt ggc tgc agg aag<br>Cys Gly Cys Arg Lys<br>100  | Asn Gln Tyr                                    |   |  | 336 |
| ttc cag tgc ttc aat<br>Phe Gln Cys Phe Asn<br>115  |  | Cys Leu Asn Gly   |  | 384 |
| tcc tgc cag gag aaa<br>Ser Cys Gln Glu Lys<br>130  |  |   |  | 432 |
| ttt cta aga gaa aac<br>Phe Leu Arg Glu Asn<br>145  |  |   |  | 480 |
| ctg gag tgc acg aag<br>Leu Glu Cys Thr Lys<br>165  |  |   |  | 528 |
| act gag gac tca ggc<br>Thr Glu Asp Ser Gly<br>180  |  |   |  | 549 |
| <210> 10<br><211> 183<br><212> PRT<br><213> Artificial Se  | quence   |   |  |     |
| <220> <223> Description o TNF-BP sequen  |  | Sequence: recomb  | inant  |     |
| <400> 10   |  |   |  |     |
| Met Leu Val Pro His<br>1 5   | _  | Arg Glu Lys Arg<br>10   | Asp Ser Val Cys<br>15  |     |
| Met Leu Val Pro His  |  | 10  | 15   |     |
| Met Leu Val Pro His  1 5  Pro Gln Gly Lys Tyr  | Ile His Pro                                    | 10<br>Gln Asn Asn Ser<br>25   | 15<br>Ile Cys Cys Thr<br>30  |     |
| Met Leu Val Pro His 1 5  Pro Gln Gly Lys Tyr 20  Lys Cys His Lys Gly   | Ile His Pro 6 Thr Tyr Leu 40                   | 10<br>Gln Asn Asn Ser<br>25<br>Tyr Asn Asp Cys                                  | Ile Cys Cys Thr<br>30<br>Pro Gly Pro Gly<br>45                           |     |
| Met Leu Val Pro His 1 5  Pro Gln Gly Lys Tyr 20  Lys Cys His Lys Gly 35  Gln Asp Thr Asp Cys                         | Thr Tyr Leu 40  Arg Glu Cys 6                  | 10  Gln Asn Asn Ser 25  Tyr Asn Asp Cys  Glu Ser Gly Ser 60                     | Ile Cys Cys Thr<br>30<br>Pro Gly Pro Gly<br>45<br>Phe Thr Ala Ser        |     |
| Met Leu Val Pro His 1 5  Pro Gln Gly Lys Tyr 20  Lys Cys His Lys Gly 35  Gln Asp Thr Asp Cys 50  Glu Asn His Leu Arg | Thr Tyr Leu 40  Arg Glu Cys 55  His Cys Leu 70 | 10  Gln Asn Asn Ser 25  Tyr Asn Asp Cys  Glu Ser Gly Ser 60  Ser Cys Ser Lys 75 | Ile Cys Cys Thr 30 Pro Gly Pro Gly 45 Phe Thr Ala Ser Cys Arg Lys Glu 80 |     |

| Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Le<br>115 120 125  | eu                 |
|--|--------------------|
| Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Ph<br>130 135 140  | ie                 |
| Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser 145 150 155  | er<br>50           |
| Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys G<br>165 170 175   | -У                 |
| Thr Glu Asp Ser Gly Thr Thr<br>180   |                    |
| <210> 11<br><211> 600<br><212> DNA<br><213> Artificial Sequence  |                    |
| <220> <223> Description of Artificial Sequence: recombinant TNF-BP sequence  |                    |
| <220> <221> CDS <222> (1)(600)   |                    |
| <pre>&lt;400&gt; 11 atg ggc ctc tcc acc gtg cct gac ctg ctg ctg cca ctg gtg ctc cc Met Gly Leu Ser Thr Val Pro Asp Leu Leu Pro Leu Val Leu Leu 1 5 10 15</pre> |                    |
| gag ctg ttg gtg gga ata tac ccc tca ggg gtt att gga gat agt g<br>Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Asp Ser Va<br>20 25 30                    |                    |
| tgt ccc caa gga aaa tat atc cac cct caa aat aat tcg att tgc tg<br>Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cy<br>35 40 45                   |                    |
| acc aag tgc cac aaa gga acc tac ttg tac aat gac tgt cca ggc co<br>Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pr                               |                    |
| 50 55 60   |                    |
| ggg cag gat acg gac tgc agg gag tgt gag agc ggc tcc ttc acc gg<br>Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr A                                |                    |
| ggg cag gat acg gac tgc agg gag tgt gag agc ggc tcc ttc acc gg<br>Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr A                                | la<br>30<br>ag 288 |

| 100   |  | 105   | *110  |     |
|---|--|---|---|-----|
| gtg tgt ggc tgc a<br>Val Cys Gly Cys A<br>115   |  |   | -33 -3- 3   | 384 |
| ctt ttc cag tgc t<br>Leu Phe Gln Cys P<br>130   |  |   | 333 3-3   | 132 |
| ctc tcc tgc cag g<br>Leu Ser Cys Gln G<br>145   |  |   |   | 180 |
| ttc ttt cta aga g<br>Phe Phe Leu Arg G<br>1   |  |   |   | 528 |
| agc ctg gag tgc a<br>Ser Leu Glu Cys T<br>180   |  |   | J - J - J   | 576 |
| ggc act gag gac t<br>Gly Thr Glu Asp S<br>195   |  |   | (   | 600 |
| <210> 12<br><211> 200<br><212> PRT<br><213> Artificial  | Sequence   |   |   |     |
| (213) Altilitial  | <b>-</b>   |   |   |     |
| <220> <223> Description TNF-BP sequ   | of Artificial  | Sequence: recomb  | oinant  |     |
| <220><br><223> Description  | of Artificial<br>dence   |   |   |     |
| <220> <223> Description TNF-BP sequence <400> 12 Met Gly Leu Ser T  | of Artificial<br>ence<br>Thr Val Pro Asp<br>5  | Leu Leu Leu Pro<br>10   | Leu Val Leu Leu<br>15   |     |
| <220> <223> Description TNF-BP sequence <400> 12 Met Gly Leu Ser T 1 Glu Leu Leu Val G  | of Artificial<br>dence<br>Thr Val Pro Asp<br>5<br>Sly Ile Tyr Pro  | Leu Leu Leu Pro<br>10<br>Ser Gly Val Ile<br>25  | Leu Val Leu Leu<br>15<br>Gly Asp Ser Val<br>30  |     |
| <220> <223> Description TNF-BP sequence <400> 12 Met Gly Leu Ser T 1 Glu Leu Leu Val G 20 Cys Pro Gln Gly L   | of Artificial Hence Thr Val Pro Asp 5 Sly Ile Tyr Pro Lys Tyr Ile His 40   | Leu Leu Leu Pro<br>10<br>Ser Gly Val Ile<br>25<br>Pro Gln Asn Asn                           | Leu Val Leu Leu 15  Gly Asp Ser Val 30  Ser Ile Cys Cys 45                                      |     |
| <220> <223> Description TNF-BP sequence <400> 12 Met Gly Leu Ser T  1 Glu Leu Leu Val G 20 Cys Pro Gln Gly I 35 Thr Lys Cys His I                         | of Artificial Hence  Thr Val Pro Asp 5  Sly Ile Tyr Pro Lys Tyr Ile His 40  Lys Gly Thr Tyr 55                     | Leu Leu Leu Pro 10  Ser Gly Val Ile 25  Pro Gln Asn Asn Leu Tyr Asn Asp 60                  | Leu Val Leu Leu 15  Gly Asp Ser Val 30  Ser Ile Cys Cys 45  Cys Pro Gly Pro                     |     |
| <220> <223> Description TNF-BP sequence <400> 12 Met Gly Leu Ser T 1  Glu Leu Leu Val G 20  Cys Pro Gln Gly L 35  Thr Lys Cys His I 50  Gly Gln Asp Thr A | of Artificial Hence  Chr Val Pro Asp 5  Gly Ile Tyr Pro Lys Tyr Ile His 40  Lys Gly Thr Tyr 55  Asp Cys Arg Glu 70 | Leu Leu Leu Pro 10 Ser Gly Val Ile 25 Pro Gln Asn Asn Leu Tyr Asn Asp 60 Cys Glu Ser Gly 75 | Leu Val Leu Leu 15  Gly Asp Ser Val 30  Ser Ile Cys Cys 45  Cys Pro Gly Pro  Ser Phe Thr Ala 80 |     |

| 11  | / Cys Arg   | Lys A                                      | Asn Glr<br>120  |                                | Arg   | His                                    | Tyr                            | Trp<br>125                                   | Ser  | Glu   | Asn                          |           |
|---|---|--|---|--------------------------------|---|--|--------------------------------|--|--|---|------------------------------|-----------|
| Leu Phe Gl:<br>130  | n Cys Phe   |  | Cys Sei<br>135  | Leu                            | Cys   | Leu                                    | Asn<br>140                     | Gly  | Thr  | Val   | His                          |           |
| Leu Ser Cy<br>145   | s Gln Glu   | Lys (                                      | Gln Asr   | Thr                            | Val   | Cys<br>155                             | Thr                            | Cys  | His  | Ala   | Gly<br>160                   |           |
| Phe Phe Le  | ı Arg Glu<br>165  |  | Glu Cys   | . Val                          | Ser<br>170  | Cys                                    | Ser                            | Asn  | Cys  | Lys<br>175  | Lys                          |           |
| Ser Leu Gl  | Cys Thr   | Lys 1                                      | Leu Cys   | Leu<br>185                     | Pro   | Gln                                    | Ile                            | Glu  | Asn<br>190                                   | Val   | Lys                          |           |
| Gly Thr Gl  | -   | Gly '                                      | Thr Thi   |                                |   |  |                                |  |  |   |                              |           |
| <210> 13<br><211> 603<br><212> DNA<br><213> Arti  | Eicial Se   | quence                                     | e   |                                |   |  |                                |  |  |   |                              |           |
| <220><br><223> Desc<br>TNF-   | ription c<br>3P sequen  |  | ificial   | . Seqi                         | uence   | e: re                                  | ecoml                          | oinar  | nt   |   |                              |           |
| <220>   |   |  |   |                                |   |  |                                |  |  |   |                              |           |
| <221> CDS<br><222> (1).   | . (603)   |  |   |                                |   |  |                                |  |  |   |                              |           |
| <221> CDS   | c tcc acc   | Val 1                                      |   |                                |   |  |                                |  |  |   |                              | 48        |
| <221> CDS<br><222> (1).<br><400> 13<br>atg ggc ct<br>Met Gly Le   | tcc acc<br>Ser Thr<br>5<br>g gtg gga  | Val :                                      | Pro Asp   | Leu<br>tca                     | Leu<br>10<br>ggg                                    | Leu<br>gtt                             | Pro<br>att                     | Leu<br>gga                                   | Val<br>ctg                                   | Leu<br>15<br>gtc                                    | Leu                          | 48<br>96  |
| <221> CDS<br><222> (1).<br><400> 13<br>atg ggc ct<br>Met Gly Le<br>1<br>gag ctg tt  | tcc acc<br>Ser Thr<br>5<br>g gtg gga<br>1 Val Gly<br>20<br>g gac agg                | ata da | Pro Asp<br>tac ccc<br>Tyr Pro   | tca<br>Ser<br>25<br>gat        | Leu<br>10<br>ggg<br>Gly<br>agt                      | Leu<br>gtt<br>Val<br>gtg               | Pro<br>att<br>Ile<br>tgt       | gga<br>Gly                                   | ctg<br>Leu<br>30                             | Leu<br>15<br>gtc<br>Val<br>gga                      | cct<br>Pro                   |           |
| <221> CDS <222> (1).  <400> 13 atg ggc ct Met Gly Le 1  gag ctg tt Glu Leu Le  cac cta gg His Leu Gl                                  | g tcc acc<br>g gtg gga<br>l Val Gly<br>20<br>g gac agg<br>y Asp Arg                 | ata di Ile di Glu di aat a                 | Pro Asp<br>tac ccc<br>Tyr Pro<br>aag aga<br>Lys Arg<br>40                             | tca<br>Ser<br>25<br>gat<br>Asp | Leu<br>10<br>ggg<br>Gly<br>agt<br>ser               | gtt<br>Val<br>gtg<br>Val               | att<br>Ile<br>tgt<br>Cys       | gga<br>Gly<br>ccc<br>Pro<br>45               | ctg<br>Leu<br>30<br>caa<br>Gln               | Leu<br>15<br>gtc<br>Val<br>gga<br>Gly<br>cac        | cct<br>Pro<br>aaa<br>Lys     | 96        |
| <221> CDS <222> (1).  <400> 13 atg ggc ct Met Gly Le     1  gag ctg tt Glu Leu Le  cac cta gg His Leu Gl     3  tat atc ca Tyr Ile Hi | g tcc acc<br>Ser Thr<br>5<br>g gtg gga<br>1 Val Gly<br>20<br>g gac agg<br>7 Asp Arg | ata da | Pro Asp<br>tac ccc<br>Tyr Pro<br>aag aga<br>Lys Arg<br>40<br>aat tcg<br>Asn Sen<br>55 | tca<br>Ser<br>25<br>gat<br>Asp | Leu<br>10<br>ggg<br>Gly<br>agt<br>Ser<br>tgc<br>Cys | gtt<br>Val<br>gtg<br>Val<br>tgt<br>Cys | Pro att Ile tgt Cys acc Thr 60 | gga<br>Gly<br>ccc<br>Pro<br>45<br>aag<br>Lys | ctg<br>Leu<br>30<br>caa<br>Gln<br>tgc<br>Cys | Leu<br>15<br>gtc<br>Val<br>gga<br>Gly<br>cac<br>His | cct<br>Pro  aaa Lys  aaa Lys | 96<br>144 |

| aga cac tgc<br>Arg His Cys   |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 336 |
|--|--|------------------|--------------------------------|--------------------------------|-------------------------|--------------------------------|--------------------------|--------------------------|--------------------------------|--------------------------------|-------------------------|-------------------|-----|
| gag atc tct<br>Glu Ile Ser<br>115  |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 384 |
| aag aac cag<br>Lys Asn Gln<br>130  |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 432 |
| aat tgc agc<br>Asn Cys Ser<br>145  |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 480 |
| aaa cag aac<br>Lys Gln Asn   |  | Cys              |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 528 |
| aac gag tgt<br>Asn Glu Cys   | -  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 576 |
| aag ttg tgc<br>Lys Leu Cys<br>195  |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   | 603 |
|  |  |                  |                                |                                |                         |                                |                          |                          |                                |                                |                         |                   |     |
| <210> 14<br><211> 201<br><212> PRT<br><213> Artif  | icial Se   | equenc           | ce                             |                                |                         |                                |                          |                          |                                |                                |                         |                   |     |
| <211> 201<br><212> PRT<br><213> Artif<br><220><br><223> Descr  |  | of Ar            |                                | cial                           | Sequ                    | ience                          | e: re                    | ecomb                    | oinar                          | ıt                             |                         |                   |     |
| <211> 201<br><212> PRT<br><213> Artif<br><220><br><223> Descr  | iption o<br>P sequer   | of Art           | tific                          |                                |                         |                                |                          |                          |                                |                                | Leu<br>15               | Leu               |     |
| <211> 201<br><212> PRT<br><213> Artif<br><220><br><223> Descr<br>TNF-B<br><400> 14<br>Met Gly Leu      | iption o<br>P sequer<br>Ser Thr  | of Artace        | tific<br>Pro                   | Asp                            | Leu                     | Leu<br>10                      | Leu                      | Pro                      | Leu                            | Val                            | 15                      |                   |     |
| <211> 201<br><212> PRT<br><213> Artif<br><220><br><223> Descr<br>TNF-B<br><400> 14<br>Met Gly Leu<br>1 | iption of P sequer  Ser Thr  Val Gly 20  | of Arrace<br>Val | Pro<br>Tyr                     | Asp<br>Pro                     | Leu<br>Ser<br>25        | Leu<br>10<br>Gly               | Leu<br>Val               | Pro<br>Ile               | Leu<br>Gly                     | Val<br>Leu<br>30               | 15<br>Val               | Pro               |     |
| <pre>&lt;211&gt; 201 &lt;212&gt; PRT &lt;213&gt; Artif &lt;220&gt; &lt;223&gt; Descr</pre>             | iption of sequents of the sequ | of Arrace<br>Val | Pro<br>Tyr<br>Lys              | Asp<br>Pro<br>Arg<br>40        | Leu<br>Ser<br>25<br>Asp | Leu<br>10<br>Gly<br>Ser        | Leu<br>Val<br>Val        | Pro<br>Ile<br>Cys        | Leu<br>Gly<br>Pro<br>45        | Val<br>Leu<br>30<br>Gln        | 15<br>Val<br>Gly        | Pro<br>Lys        |     |
| <211> 201 <212> PRT <213> Artif <220> <223> Descr  | iption of sequents of sequents of the sequents | of Arrace Val    | Pro<br>Tyr<br>Lys<br>Asn<br>55 | Asp<br>Pro<br>Arg<br>40<br>Ser | Leu<br>Ser<br>25<br>Asp | Leu<br>10<br>Gly<br>Ser<br>Cys | Leu<br>Val<br>Val<br>Cys | Pro<br>Ile<br>Cys<br>Thr | Leu<br>Gly<br>Pro<br>45<br>Lys | Val<br>Leu<br>30<br>Gln<br>Cys | 15<br>Val<br>Gly<br>His | Pro<br>Lys<br>Lys |     |

|  | Leu Ser<br>100   | Cys Ser  | Lys Cy<br>10  |  | Lys Gl                                       | ı Met  | Gly<br>110                                   | Gln                                   | Val                 |                 |
|--|--|--|---|--|--|--|--|---------------------------------------|---------------------|-----------------|
| Glu Ile Ser<br>115   | Ser Cys  | Thr Val  | Asp Ar<br>120   | g Asp  | Thr Va                                       | l Cys<br>125                                       | Gly  | Cys                                   | Arg                 |                 |
| Lys Asn Gln<br>130   | Tyr Arg  | His Tyr<br>135   | Trp Se  | er Glu   | Asn Let                                      |  | Gln  | Cys                                   | Phe                 |                 |
| Asn Cys Ser<br>145   | Leu Cys  | Leu Asn<br>150   | Gly Th  | r Val  | His Let<br>155                               | ı Ser  | Cys  | Gln                                   | Glu<br>160          |                 |
| Lys Gln Asn  | Thr Val<br>165   | Cys Thr  | Суѕ Ні  | .s Ala<br>170  | Gly Pho                                      | e Phe  | Leu  | Arg<br>175                            | Glu                 |                 |
| Asn Glu Cys  | Val Ser<br>180   | Cys Ser  | Asn Cy<br>18  |  | Lys Se                                       | c Leu  | Glu<br>190                                   | Cys                                   | Thr                 |                 |
| Lys Leu Cys<br>195   | Leu Pro  | Gln Ile  | Glu As<br>200   | sn   |  |  |  |                                       |                     |                 |
| <210> 15<br><211> 519<br><212> DNA<br><213> Artif  | icial Se   | quence   |   |  |  |  |  |                                       |                     |                 |
| <220>  |  |  |   |  |  |  |  |                                       |                     |                 |
| <223> Descr<br>TNF-B   | iption o<br>P sequen   |  | cial Se   | equence  | e: reco                                      | mbinan   | nt   |                                       |                     |                 |
|  | P sequen   |  | cial Se   | equence  | e: reco                                      | mbinan   | nt   |                                       |                     |                 |
| TNF-B <220> <221> CDS <222> (1) <400> 15   | P sequen   | ce   |   |  |  |  |  | gtg                                   | tgt                 | 48              |
| TNF-B <220> <221> CDS <222> (1)  | P sequent<br>(519)<br>cct cac  | ce<br>cta ggg  | gac aç  | id ded   | aag ag                                       | a gat  | agt  |                                       |                     | 48              |
| <pre>TNF-B &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; (1) &lt;400&gt; 15 atg ctg gtc Met Leu Val</pre>                | P sequent<br>(519)<br>cct cac<br>Pro His<br>5<br>aaa tat                         | cta ggg<br>Leu Gly<br>atc cac                                  | gac aq<br>Asp Ai<br>cct ca<br>Pro Gl                  | gg gag<br>gg Glu<br>10   | aag ag.<br>Lys Ard                           | a gat<br>J Asp                                     | agt<br>Ser<br>tgc                            | Val<br>15<br>tgt                      | Cys                 | <b>48</b><br>96 |
| TNF-B <220> <221> CDS <222> (1) <400> 15 atg ctg gtc Met Leu Val 1 ccc caa gga                                     | P sequent (519)  cct cac Pro His 5  aaa tat Lys Tyr 20  aaa gga Lys Gly          | cta ggg<br>Leu Gly<br>atc cac<br>Ile His                       | gac ag<br>Asp An<br>cct ca<br>Pro Gl                  | gg gag<br>rg Glu<br>10<br>aa aat<br>ln Asn<br>25                     | aag aga<br>Lys Ard<br>aat to<br>Asn Se       | a gat<br>g Asp<br>g att<br>r Ile                   | agt<br>Ser<br>tgc<br>Cys<br>30               | Val<br>15<br>tgt<br>Cys               | Cys<br>acc<br>Thr   |                 |
| TNF-B <220> <221> CDS <222> (1) <400> 15 atg ctg gtc Met Leu Val 1 ccc caa gga Pro Gln Gly aag tgc cac Lys Cys His | P sequent (519)  cct cac Pro His 5  aaa tat Lys Tyr 20  aaa gga Lys Gly  gac tgc | cta ggg<br>Leu Gly<br>atc cac<br>Ile His<br>acc tac<br>Thr Tyr | gac ag Asp An cct ca Pro Gl 2 ttg ta Leu Ty 40 tgt ga | gg gag<br>gg Glu<br>10<br>aa aat<br>ln Asn<br>25<br>ac aat<br>yr Asn | aag ag. Lys Arc aat tc Asn Se. gac tg Asp Cy | a gat g Asp g att r Ile t cca s Pro 45 c ttc r Phe | agt<br>Ser<br>tgc<br>Cys<br>30<br>ggc<br>Gly | Val<br>15<br>tgt<br>Cys<br>ccg<br>Pro | Cys acc Thr ggg Gly | 96              |

| atg g<br>Met G                            |  |                                |                            |   |                              |                                |                                |                            |                                       |                                       |                                       |                                |                         | acc<br>Thr<br>95                            |                        | 288 |
|---|--|--------------------------------|----------------------------|---|------------------------------|--------------------------------|--------------------------------|----------------------------|---------------------------------------|---------------------------------------|---------------------------------------|--------------------------------|-------------------------|---|------------------------|-----|
| tgt g<br>Cys G                            |  |                                |                            |   |                              |                                |                                |                            |                                       |                                       |                                       |                                |                         |   |                        | 336 |
| ttc c                                     | _  | _                              |                            |   | _                            | _                              |                                |                            |                                       |                                       |                                       |                                |                         |   |                        | 384 |
| tcc t<br>Ser C                            |  |                                |                            |   |                              |                                |                                |                            |                                       |                                       |                                       |                                |                         |   |                        | 432 |
| ttt c<br>Phe I<br>145                     |  |                                |                            |   |                              |                                |                                |                            |                                       |                                       |                                       |                                |                         |   |                        | 480 |
| ctg g<br>Leu G                            |  |                                |                            |   |                              |                                |                                |                            |                                       |                                       |                                       |                                |                         |   |                        | 519 |
| <210><211><211><212><213>                 | > 17<br>> PF   | '3<br>RT                       | lcial                      | l Sec   | quenc                        | ce                             |                                |                            |                                       |                                       |                                       |                                |                         |   |                        |     |
|   |  |                                |                            |   | _                            |                                |                                |                            |                                       |                                       |                                       |                                |                         |   |                        |     |
| <220><br><223>                            | > De   |                                | ptic                       |   | E Art                        |                                | cial                           | Seqi                       | ience                                 | e: re                                 | ecomb                                 | oinar                          | ıt                      |   |                        |     |
|   | > De<br>TN<br>> 16                                   | 1F-BI                          | lptic<br>P sec             | on of<br>quenc  | E Art                        | ific                           |                                |                            |                                       |                                       |                                       |                                |                         | Val<br>15                                   | Cys                    |     |
| <223>                                     | > De<br>TN<br>> 16<br>Leu                            | IF-BI<br>Val                   | iptic<br>Psec              | on of<br>quenc<br>His<br>5                              | E Art<br>ce<br>Leu           | cific                          | Asp                            | Arg                        | Glu<br>10                             | Lys                                   | Arg                                   | Asp                            | Ser                     | 15  |                        |     |
| <223> <400> Met I                         | > De<br>TN<br>> 16<br>Leu<br>Gln                     | IF-BI<br>Val<br>Gly            | Pro Lys                    | on of<br>quenc<br>His<br>5<br>Tyr                       | E Art<br>ce<br>Leu<br>Ile    | Gly<br>His                     | Asp<br>Pro                     | Arg<br>Gln<br>25           | Glu<br>10<br>Asn                      | Lys<br>Asn                            | Arg<br>Ser                            | Asp<br>Ile                     | Ser<br>Cys<br>30        | 15<br>Cys                                   | Thr                    |     |
| <223> <400> Met I 1 Pro G                 | > De<br>TN<br>> 16<br>Leu<br>Gln                     | Val<br>Gly<br>His<br>35        | Pro Lys 20 Lys             | on of<br>quenc<br>His<br>5<br>Tyr                       | E Art                        | Gly<br>His                     | Asp<br>Pro<br>Leu<br>40        | Arg Gln 25 Tyr             | Glu<br>10<br>Asn<br>Asn               | Lys<br>Asn<br>Asp                     | Arg<br>Ser<br>Cys                     | Asp<br>Ile<br>Pro<br>45        | Ser<br>Cys<br>30<br>Gly | 15<br>Cys<br>Pro                            | Thr                    |     |
| <223> <400> Met I  1  Pro G               | > De<br>TN<br>> 16<br>Leu<br>Gln<br>Cys<br>Asp       | Val<br>Gly<br>His<br>35        | Pro Lys 20 Lys Asp         | on of<br>quence<br>His<br>5<br>Tyr<br>Gly<br>Cys        | E Artce Leu Ile Thr          | Gly<br>His<br>Tyr<br>Glu<br>55 | Asp<br>Pro<br>Leu<br>40<br>Cys | Arg Gln 25 Tyr             | Glu<br>10<br>Asn<br>Asn               | Lys<br>Asn<br>Asp<br>Gly              | Arg<br>Ser<br>Cys<br>Ser<br>60        | Asp<br>Ile<br>Pro<br>45<br>Phe | Ser Cys 30 Gly          | 15<br>Cys<br>Pro<br>Ala                     | Thr<br>Gly<br>Ser      |     |
| <223> <400> Met I  1  Pro G  Lys C  Gln A | > De<br>TN<br>> 16<br>Leu<br>Gln<br>Cys<br>Asp<br>50 | Val<br>Gly<br>His<br>35<br>Thr | Pro Lys 20 Lys Asp         | on of<br>quence<br>His<br>5<br>Tyr<br>Gly<br>Cys        | E Artice Leu Ile Thr Arg His | Gly His Tyr Glu 55             | Asp Pro Leu 40 Cys             | Arg Gln 25 Tyr Glu Ser     | Glu<br>10<br>Asn<br>Asn<br>Ser        | Lys<br>Asn<br>Asp<br>Gly<br>Ser<br>75 | Arg<br>Ser<br>Cys<br>Ser<br>60<br>Lys | Asp Ile Pro 45 Phe Cys         | Ser Cys 30 Gly Thr      | 15<br>Cys<br>Pro<br>Ala<br>Lys              | Thr Gly Ser Glu 80     |     |
| <223> <400> Met I                         | > De<br>TN<br>> 16<br>Leu<br>Cys<br>Asp<br>50<br>Asn | Val<br>Gly<br>His<br>35<br>Thr | Pro Lys 20 Lys Asp Leu Val | on of<br>quence<br>His<br>5<br>Tyr<br>Gly<br>Cys<br>Arg | Leu Ile Thr Arg His 70       | Gly His Tyr Glu 55 Cys         | Asp Pro Leu 40 Cys Leu Ser     | Arg Gln 25 Tyr Glu Ser Cys | Glu<br>10<br>Asn<br>Asn<br>Ser<br>Cys | Lys Asn Asp Gly Ser 75                | Arg Ser Cys Ser 60 Lys Asp            | Asp Ile Pro 45 Phe Cys         | Ser Cys 30 Gly Thr Arg  | 15<br>Cys<br>Pro<br>Ala<br>Lys<br>Thr<br>95 | Thr Gly Ser Glu 80 Val |     |

| Ser Cys Gln Glu Lys Gln Asn T  |                          | Cys His Ala Gly P<br>140 | ?he        |
|--|--------------------------|--------------------------|------------|
| Phe Leu Arg Glu Asn Glu Cys V<br>145 150                                 | Val Ser Cys Ser A<br>155 |                          | Ser<br>160 |
| Leu Glu Cys Thr Lys Leu Cys I<br>165                                     | Leu Pro Gln Ile G<br>170 | Glu Asn                  |            |
| <210> 17<br><211> 570<br><212> DNA<br><213> Artificial Sequence          |                          |                          |            |
| <220> <223> Description of Artifici TNF-BP sequence                      | ial Sequence: rec        | combinant                |            |
| <220> <221> CDS <222> (1)(570)   |                          |                          |            |
| <400> 17 atg ggc ctc tcc acc gtg cct g Met Gly Leu Ser Thr Val Pro A 1 5 |                          |                          |            |
| gag ctg ttg gtg gga ata tac c<br>Glu Leu Leu Val Gly Ile Tyr E<br>20     |                          |                          |            |
| tgt ccc caa gga aaa tat atc c<br>Cys Pro Gln Gly Lys Tyr Ile F<br>35     |                          |                          |            |
| acc aag tgc cac aaa gga acc t<br>Thr Lys Cys His Lys Gly Thr T<br>50 55  |                          | Asp Cys Pro Gly P        |            |
| ggg cag gat acg gac tgc agg g<br>Gly Gln Asp Thr Asp Cys Arg 6<br>65 70  |                          |                          |            |
| tca gaa aac cac ctc aga cac t<br>Ser Glu Asn His Leu Arg His C<br>85     |                          |                          |            |
| gaa atg ggt cag gtg gag atc t<br>Glu Met Gly Gln Val Glu Ile S<br>100    |                          |                          |            |
| gtg tgt ggc tgc agg aag aac c<br>Val Cys Gly Cys Arg Lys Asn C<br>115    |                          |                          |            |

| ctt<br>Leu                   |               | _          | _          |                |            | _          | _          |            | _         |            |            |            |            | -         |            | 432 |
|------------------------------|---------------|------------|------------|----------------|------------|------------|------------|------------|-----------|------------|------------|------------|------------|-----------|------------|-----|
| ctc<br>Leu<br>145            |               | _          | _          |                |            | _          |            |            |           | _          |            | _          |            | _         |            | 480 |
| ttc<br>Phe                   |               |            |            |                |            |            |            |            |           |            |            |            |            |           |            | 528 |
| agc<br>Ser                   | -             |            | _          | _              | _          | _          | _          |            |           | _          |            |            |            |           |            | 570 |
| <210<br><211<br><212<br><213 | > 19<br> > PF | 90<br>RT   | icia:      | l Sed          | quenc      | ce         |            |            |           |            |            |            |            |           |            |     |
| <220<br><223                 | > De          |            | _          | on of<br>quenc |            | cific      | cial       | Seq        | ıence     | e: re      | ecomb      | oinar      | nt         |           |            |     |
| <400<br>Met<br>1             |               |            | Ser        | Thr<br>5       | Val        | Pro        | Asp        | Leu        | Leu<br>10 | Leu        | Pro        | Leu        | Val        | Leu<br>15 | Leu        |     |
| Glu                          | Leu           | Leu        | Val<br>20  | Gly            | Ile        | Tyr        | Pro        | Ser<br>25  | Gly       | Val        | Ile        | Gly        | Asp<br>30  | Ser       | Val        |     |
| Cys                          | Pro           | Gln<br>35  | Gly        | Lys            | Tyr        | Ile        | His<br>40  | Pro        | Gln       | Asn        | Asn        | Ser<br>45  | Ile        | Cys       | Суз        |     |
| Thr                          | Lys<br>50     | Cys        | His        | Lys            | Gly        | Thr<br>55  | Tyr        | Leu        | Tyr       | Asn        | Asp<br>60  | Cys        | Pro        | Gly       | Pro        |     |
| Gly<br>65                    | Gln           | Asp        | Thr        | Asp            | Cys<br>70  | Arg        | Glu        | Cys        | Glu       | Ser<br>75  | Gly        | Ser        | Phe        | Thr       | Ala<br>80  |     |
| Ser                          | Glu           | Asn        | His        | Leu<br>85      | Arg        | His        | Cys        | Leu        | Ser<br>90 | Cys        | Ser        | Lys        | Cys        | Arg<br>95 | Lys        |     |
| Glu                          | Met           | Gly        | Gln<br>100 | Val            | Glu        | Ile        | Ser        | Ser<br>105 | Cys       | Thr        | Val        | Asp        | Arg<br>110 | Asp       | Thr        |     |
| Val                          | Cys           | Gly<br>115 | Cys        | Arg            | Lys        | Asn        | Gln<br>120 | Tyr        | Arg       | His        | Tyr        | Trp<br>125 | Ser        | Glu       | Asn        |     |
| Leu                          | Phe<br>130    | Gln        | Cys        | Phe            | Asn        | Cys<br>135 | Ser        | Leu        | Cys       | Leu        | Asn<br>140 | Gly        | Thr        | Val       | His        |     |
| Leu<br>145                   | Ser           | Cys        | Gln        | Glu            | Lys<br>150 | Gln        | Asn        | Thr        | Val       | Cys<br>155 | Thr        | Cys        | His        | Ala       | Gly<br>160 |     |

Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys 165 170 175

Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile Glu Asn 180 185 190

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48

96

144

192

288

tgg agt gaa aac ctt ttc cag tgc ttc aat tgc agc ctc tgc ctc aat 336
Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn 100

ggg acc gtg cac ctc tcc tgc cag gag aaa cag aac acc gtg tgc acc 384
Gly Thr Val His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr 115

tgc cat gca ggt ttc ttt cta aga gaa aac gag tgt gtc tcc tgt agt 432
Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser 130

| aac tgt aag aaa agc ctg gag tgc acg aag ttg tgc cta ccc cag att Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile 145 150 155 160 |
|---|
| gag aat gtt aag ggc act gag gac tca ggc acc aca<br>Glu Asn Val Lys Gly Thr Glu Asp Ser Gly Thr Thr<br>165 170                                   |
| <210> 20<br><211> 172<br><212> PRT<br><213> Artificial Sequence   |
| <220> <223> Description of Artificial Sequence: recombinant TNF-BP sequence   |
| <pre>&lt;400&gt; 20 Met Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn 1 5 10 15</pre>   |
| Ser Ile Cys Cys Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp<br>20 25 30   |
| Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly 35 40 45  |
| Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser 50 55 60  |
| Lys Cys Arg Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val<br>65 70 75 80  |
| Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr 85 90 95  |
| Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn 100 105 110   |
| Gly Thr Val His Leu Ser Cys Gln Glu Lys Gln Asn Thr Val Cys Thr<br>115 120 125  |
| Cys His Ala Gly Phe Phe Leu Arg Glu Asn Glu Cys Val Ser Cys Ser<br>130 135 140  |
| Asn Cys Lys Lys Ser Leu Glu Cys Thr Lys Leu Cys Leu Pro Gln Ile<br>145 150 155 160  |

Glu Asn Val Lys Gly Thr Glu Asp Ser Gly Thr Thr

165

480

516

<210> 21 <211> 1334 <212> DNA 170

## <213> Artificial Sequence <220> <223> Description of Artificial Sequence: cDNA insert of lambdaTNF-BP15 and pTNF-BP15 vectors <220> <221> CDS <222> (213)..(1325) <400> 21 quattetetg gaetgagget ceagttetgg cetttggggt teaagateae tgggaecagg 60 ccgtgatctc tatgcccgag tctcaaccct caactgtcac cccaaggcac ttgggacgtc 120 ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180 233 aatgggcgag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct Met Gly Leu Ser Thr Val Pro 281 gac ctg ctg cca ctg gtg ttc ctg gag ctg ttg gtg gga ata tac Asp Leu Leu Pro Leu Val Phe Leu Glu Leu Val Gly Ile Tyr 10 15 329 ccc tca ggg gtt att gga ctg gtc cct cac cta ggg gac agg gag aag Pro Ser Gly Val Ile Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys 25 30 35 aga gat agt gtg tgt ccc caa gga aaa tat atc cac cct caa aat aat 377 Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn 40 50 tcg att tgc tgt acc aag tgc cac aaa gga acc tac ttg tac aat gac 425 Ser Ile Cys Cys Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp 473 tgt cca ggc ccg ggg cag gat acg gac tgc agg gag tgt gag agc ggc Cys Pro Gly Pro Gly Gln Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly 75 tcc ttc acc gct tca gaa aac cac ctc aga cac tgc ctc agc tgc tcc 521 Ser Phe Thr Ala Ser Glu Asn His Leu Arg His Cys Leu Ser Cys Ser 100 90 95 569 aaa tqc cga aag gaa atc ggt cag gtg gag atc tct tct tgc aca gtg Lys Cys Arg Lys Glu Ile Gly Gln Val Glu Ile Ser Ser Cys Thr Val 110 105 gac cgg gac acc gtg tgt ggc tgc agg aag aac cag tac cgg cat tat 617 Asp Arg Asp Thr Val Cys Gly Cys Arg Lys Asn Gln Tyr Arg His Tyr 135 120 125 tgg agt gaa aac ctt ttc cag tgc ttc aat tgc agc ctc tgc ctc aat 665 Trp Ser Glu Asn Leu Phe Gln Cys Phe Asn Cys Ser Leu Cys Leu Asn 145 140

| Gly Thr Val H                         |   | Lys Gln Asn     | acc gtg tgc a<br>Thr Val Cys 1<br>165        |      |
|---------------------------------------|---|-----------------|--|------|
|                                       |   |                 | gtc tcc tgt a<br>Val Ser Cys S<br>180        |      |
|                                       |   | <br>            | cta ccc cag a<br>Leu Pro Gln 1               |      |
|                                       |   |                 | gtg ctg ttg c<br>Val Leu Leu I               |      |
|                                       |   |                 | ctc ttc att c<br>Leu Phe Ile (<br>230        |      |
| Leu Met Tyr A                         | _ | <br>Ser Lys Leu | tac tcc att of<br>Tyr Ser Ile V<br>245       |      |
|                                       |   |                 | gaa gga act a<br>Glu Gly Thr 1<br>260        |      |
|                                       |   |                 | act cca ggc t<br>Thr Pro Gly I               |      |
|                                       |   | <br>-           | acc ttc acc t<br>Thr Phe Thr S               |      |
| -                                     |   |                 | gcg gct ccc of Ala Ala Pro A                 |      |
| Arg Glu Val A                         | - | <br>Ala Asp Pro | atc ctt gcg a<br>Ile Leu Ala 1<br>325        |      |
| -                                     |   |                 | aag tgg gag g<br>Lys Trp Glu <i>P</i><br>340 |      |
|                                       |   |                 | ccc gcg acg c<br>Pro Ala Thr I               |      |
| tac gcc gtg g<br>Tyr Ala Val V<br>360 |   | <br>            | aaggaattc                                    | 1334 |

| <210> 22<br><211> 371<br><212> PRT<br><213> Artificial Sequence                                     |
|---|
| <220> <223> Description of Artificial Sequence: cDNA insert of lambdaTNF-BP15 and pTNF-BP15 vectors |
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| Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly Leu Val Pro 20 25 30                            |
| His Leu Gly Asp Arg Glu Lys Arg Asp Ser Val Cys Pro Gln Gly Lys 35 40 45                            |
| Tyr Ile His Pro Gln Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys 50 55 60                            |
| Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln Asp Thr Asp 65 70 75 80                         |
| Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn His Leu<br>85 90 95                         |
| Arg His Cys Leu Ser Cys Ser Lys Cys Arg Lys Glu Ile Gly Gln Val                                     |
| Glu Ile Ser Ser Cys Thr Val Asp Arg Asp Thr Val Cys Gly Cys Arg<br>115 120 125                      |
| Lys Asn Gln Tyr Arg His Tyr Trp Ser Glu Asn Leu Phe Gln Cys Phe<br>130 135 140                      |
| Asn Cys Ser Leu Cys Leu Asn Gly Thr Val His Leu Ser Cys Gln Glu<br>145 150 155 160                  |
| Lys Gln Asn Thr Val Cys Thr Cys His Ala Gly Phe Phe Leu Arg Glu<br>165 170 175                      |
| Asn Glu Cys Val Ser Cys Ser Asn Cys Lys Lys Ser Leu Glu Cys Arg<br>180 185 190                      |
| Lys Leu Cys Leu Pro Gln Ile Glu Asn Val Lys Gly Thr Glu Asp Ser<br>195 200 205                      |
| Gly Thr Thr Val Leu Leu Pro Leu Val Ile Phe Phe Gly Leu Cys Leu 210 215 220                         |
| Leu Ser Leu Leu Phe Ile Gly Leu Met Tyr Arg Tyr Gln Arg Trp Lys<br>225 230 235 240                  |
| Ser Lys Leu Tyr Ser Ile Val Cys Gly Lys Ser Thr Pro Glu Lys Glu<br>245 250 255                      |

Gly Glu Leu Glu Gly Thr Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser 265 Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val 280 Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys 300 295 Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly 315 Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn 330 325 Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp 345 Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro 360 Leu Arg Trp 370 <210> 23 <211> 6414 <212> DNA <213> Artificial Sequence <220> <223> Description of Artificial Sequence: pADCMV1 vector <220> <221> unsure <222> (344) <223> "n" can be a, g, c, or t <220> <221> unsure <222> (4157) <223> "n" can be a, g, c, or t <220> <221> unsure <222> (5135) <223> "n" can be a, g, c, or t <220> <221> unsure <222> (6255) <223> "n" can be a, g, c, or t tcgacattga ttattgacta gttattaata gtaatcaatt acggggtcat tagttcatag 60 cccatatatg gagttccgcg ttacataact tacggtaaat ggcccgcctc gctgaccgcc 120 caacgacccc cgcccattga cgtcaataat gacgtatgtt cccatagtaa cgccaatagg 180 gactttccat tgacgtcaat gggtggagta tttacggtaa actgcccact tggcagtaca 240 tcaagtgtat catatgccaa gtacgccccc tattgacgtc aatgacggta aatggcccgc 300 ctggcattat gcccagtaca tgaccttatg ggactttcct actnggcagt acatctacgt 360 attagtcatc gctattacca tggtgatgcg gttttggcag tacatcaatg ggcgtggata 420 gcggtttgac tcacggggat ttccaagtct ccaccccatt gacgtcaatg ggagtttgtt 480 ttggcaccaa aatcaacggg actttccaaa atgtcgtaac aactccgccc cattgacgca 540 aatgggcggt aggcgtgtac ggtgggaggt ctatataagc agagctctct ggctaactag 600 agaacccact gettaactgg ettategaaa ttaatacgae teactatagg gagacccaag 660 cttctgcagg tcgacatcga tggatccggt acctcgagcg cgaattctct agaggatctt 720 tgtgaaggaa ccttacttct gtggtgtgac ataattggac aaactaccta cagagattta 780 aagetetaag gtaaatataa aatttttaag tgtataatgt gttaaaetae tgattetaat 840 tgtttgtgta ttttagattc caacctatgg aactgatgaa tgggagcagt ggtggaatgc 900 ctttaatgag gaaaacctgt tttgctcaga agaaatgcca tctagtgatg atgaggctac 960 tgctgactct caacattcta ctcctccaaa aaagaagaga aaggtagaag accccaagga 1020 ctttccttca gaattgctaa gttttttgag tcatgctgtg tttagtaata gaactcttgc 1080 ttgctttgct atttacacca caaaggaaaa agctgcactg ctatacaaga aaattatgga 1140 aaaatatttg atgtatagtg ccttgactag agatcataat cagccatacc acatttgtag 1200 aggttttact tgctttaaaa aacctcccac acctcccct gaacctgaaa cataaaatga 1260 atgcaattgt tgttgttaac ttgtttattg cagcttataa tggttacaaa taaagcaata 1320 gcatcacaaa tttcacaaat aaagcatttt tttcactgca ttctagttgt ggtttgtcca 1380 aactcatcaa tgtatcttat catgtctgga tcaattctga gaaactagcc ttaaagacag 1440 acagctttgt tctagtcagc caggcaagca tatgtaaata aagttcctca gggaactgag 1500 gttaaaagat gtatcctgga cctgccagac ctggccattc acgtaaacag aagattccgc 1560 ctcaagttcc ggttaacaac aggaggcaac gagatctcaa atctattact tctaatcggg 1620 taattaaaac ctttcaacta aaacacggac ccacggatgt cacccacttt tccttccccg 1680 geteegeest teteagtast coccaccatt aggetegeta etecacetee aetteeggge 1740 gcgacaccca cgtgccctct cccacccgac gctaaccccg ccctgcccg tctgaccccg 1800

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| gggctcacgc tgccaacacc cgggccacct ggtccgatcg tcttacttca ttcaccagcg 180   | 0 |
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| ggac atg ggt ctc ccc atc gtg cct ggc ctg ctg ctg tca ctg gtg ctc 289  Met Gly Leu Pro Ile Val Pro Gly Leu Leu Leu Ser Leu Val Leu  1 5 10 15              | 9 |
| ctg gct ctg ctg atg ggg ata cac cca tca ggg gtc acc gga ctg gtt 337 Leu Ala Leu Leu Met Gly Ile His Pro Ser Gly Val Thr Gly Leu Val 20 25 30              | 7 |
| cct tct ctt ggt gac cgg gag aag agg gat aat ttg tgt ccc cag gga 385 Pro Ser Leu Gly Asp Arg Glu Lys Arg Asp Asn Leu Cys Pro Gln Gly 35 40 45              | 5 |
| aag tat gcc cat cca aag aat aat tcc atc tgc tgc acc aag tgc cac 433 Lys Tyr Ala His Pro Lys Asn Asn Ser Ile Cys Cys Thr Lys Cys His 50 55 60              | 3 |
| aaa gga acc tac ttg gtg agt gac tgt cca agc cca ggg cag gaa aca 481<br>Lys Gly Thr Tyr Leu Val Ser Asp Cys Pro Ser Pro Gly Gln Glu Thr<br>65 70 75        | 1 |
| gtc tgc gag ctc tct cat aaa ggc acc ttt aca gct tcg cag aac cac 529 Val Cys Glu Leu Ser His Lys Gly Thr Phe Thr Ala Ser Gln Asn His 80 85 90 95           | 9 |
| gtc aga cag tgt ctc agt tgc aag aca tgt cgg aaa gaa atg ttc cag 577 Val Arg Gln Cys Leu Ser Cys Lys Thr Cys Arg Lys Glu Met Phe Gln 100 105 110           | 7 |
| gtg gag att tot oot tgo aaa got gac atg gac acc gtg tgt ggc tgc 625<br>Val Glu Ile Ser Pro Cys Lys Ala Asp Met Asp Thr Val Cys Gly Cys<br>115 120 125     | 5 |
| aag aag aac caa ttc cag cgc tac ctg agt gag acg cat ttc cag tgt 673<br>Lys Lys Asn Gln Phe Gln Arg Tyr Leu Ser Glu Thr His Phe Gln Cys<br>130 135 140     | 3 |
| gtg gac tgc agc ccc tgc ttc aat ggc acc gtg aca atc ccc tgt aag 721 Val Asp Cys Ser Pro Cys Phe Asn Gly Thr Val Thr Ile Pro Cys Lys 145 150 155           | 1 |
| gag aaa cag aac acc gtg tgt aac tgc cac gca gga ttc ttt cta agc 769<br>Glu Lys Gln Asn Thr Val Cys Asn Cys His Ala Gly Phe Phe Leu Ser<br>160 165 170 175 | 9 |
| gga aat gag tgc acc cct tgc agc cac tgc aag aaa aat cag gaa tgt 817<br>Gly Asn Glu Cys Thr Pro Cys Ser His Cys Lys Lys Asn Gln Glu Cys<br>180 185 190     | 7 |
| atg aag ctg tgc cta cct cca gtt gca aat gtc aca aac ccc cag gac  Met Lys Leu Cys Leu Pro Pro Val Ala Asn Val Thr Asn Pro Gln Asp  195 200 205             | 5 |

| tca g<br>Ser G          |       | nr Ala |       |   |   |  |   |   |  |   | 913  |
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| ctt t<br>Leu Le<br>2    |       |        |       |   |   |  |   |   |  |   | 961  |
| agg co<br>Arg P:<br>240 |       |        |       |   |   |  |   |   |  |   | 1009 |
| gag g<br>Glu V          |       |        |       |   |   |  |   |   |  |   | 1057 |
| atc co                  |       |        | e Ser |   |   |  |   |   |  |   | 1105 |
| agc a<br>Ser T          | hr Th |        | _     |   | _ |  | _ | - |  |   | 1153 |
| ccc g<br>Pro V          |       |        |       | _ |   |  |   |   |  | _ | 1201 |
| gag g<br>Glu V<br>320   |       |        |       |   |   |  |   |   |  |   | 1249 |
| aac c                   |       |        |       |   |   |  |   |   |  |   | 1297 |
| gcg g                   |       |        | Gln   |   |   |  |   |   |  |   | 1345 |
| gct g<br>Ala V          |       | al Asp |       |   |   |  |   |   |  |   | 1393 |
| ctc c<br>Leu L          |       |        |       |   |   |  |   |   |  |   | 1441 |
| ggg ce<br>Gly A<br>400  |       |        |       |   |   |  |   |   |  |   | 1489 |
| cgc c                   |       |        |       |   |   |  |   |   |  |   | 1537 |

| ctt tgc gac atg aac ctg cgt ggc tgc ctg gag aac atc cgc gag act 15 Leu Cys Asp Met Asn Leu Arg Gly Cys Leu Glu Asn Ile Arg Glu Thr 435 440 445 | 85  |
|--|-----|
| cta gaa agc cct gcc cac tcg tcc acg acc cac ctc ccg cga Leu Glu Ser Pro Ala His Ser Ser Thr Thr His Leu Pro Arg 450 455 460                    | 27  |
| taaggccaca cccccacctc aggaacggga ctcgaaggac catcctgcta gatgccctgc 16   | 87  |
| ttccctgtga acctcctctt tggtcctcta gggggcaggc tcgatctggc aggctcgatc 17   | 47  |
| tggcagccac ttccttggtg ctaccgactt ggtgtacata gcttttccca gctgccgagg 18   | 307 |
| acageetgtg ecageeactt gtgeatggea gggaagtgtg ecatetgete ecagaeaget 18   | 867 |
| gagggtgcca aaagccagga gaggtgattg tggagaaaaa gcacaatcta tctgataccc 19   | 27  |
| acttgggatg caaggaccca aacaaagctt ctcagggcct cctcagttga tttctgggcc 19   | 87  |
| cttttcacag tagataaaac agtctttgta ttgattatat cacactaatg gatgaacggt 20   | 47  |
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Ser Leu Gly Asp Arg Glu Lys Arg Asp Asn Leu Cys Pro Gln Gly Lys 35 40 45

Tyr Ala His Pro Lys Asn Asn Ser Ile Cys Cys Thr Lys Cys His Lys 50 55 60

Gly Thr Tyr Leu Val Ser Asp Cys Pro Ser Pro Gly Gln Glu Thr Val 65 70 75 80

Cys Glu Leu Ser His Lys Gly Thr Phe Thr Ala Ser Gln Asn His Val 85 90 95

Arg Gln Cys Leu Ser Cys Lys Thr Cys Arg Lys Glu Met Phe Gln Val

|                    | 100            |                |            | 105        |            |            |            |            | 110        |            |            |
|--------------------|----------------|----------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Glu Ile Ser<br>115 | _              | Lys Ala        | Asp<br>120 | Met        | Asp        | Thr        | Val        | Cys<br>125 | Gly        | Cys        | Lys        |
| Lys Asn Glr<br>130 | n Phe Gln      | Arg Tyr<br>135 | Leu        | Ser        | Glu        | Thr        | His<br>140 | Phe        | Gln        | Cys        | Val        |
| Asp Cys Ser<br>145 | Pro Cys        | Phe Asn<br>150 | Gly        | Thr        | Val        | Thr<br>155 | Ile        | Pro        | Cys        | Lys        | Glu<br>160 |
| Lys Gln Asr        | Thr Val<br>165 | _              | Суз        | His        | Ala<br>170 | Gly        | Phe        | Phe        | Leu        | Ser<br>175 | Gly        |
| Asn Glu Cys        | Thr Pro        | Cys Ser        | His        | Cys<br>185 | Lys        | Lys        | Asn        | Gln        | Glu<br>190 | Cys        | Met        |
| Lys Leu Cys<br>195 |                | Pro Val        | Ala<br>200 | Asn        | Val        | Thr        | Asn        | Pro<br>205 | Gln        | Asp        | Ser        |
| Gly Thr Ala<br>210 | a Val Leu      | Leu Pro<br>215 | Leu        | Val        | Ile        | Phe        | Leu<br>220 | Gly        | Leu        | Сув        | Leu        |
| Leu Phe Phe<br>225 | e Ile Cys      | Ile Ser<br>230 | Leu        | Leu        | Cys        | Arg<br>235 | Tyr        | Pro        | Gln        | Trp        | Arg<br>240 |
| Pro Arg Val        | Tyr Ser<br>245 |                | Cys        | Arg        | Asp<br>250 | Ser        | Ala        | Pro        | Val        | Lys<br>255 | Glu        |
| Val Glu Gly        | Glu Gly<br>260 | Ile Val        | Thr        | Lys<br>265 | Pro        | Leu        | Thr        | Pro        | Ala<br>270 | Ser        | Ile        |
| Pro Ala Phe<br>275 |                | Asn Pro        | Gly<br>280 | Phe        | Asn        | Pro        | Thr        | Leu<br>285 | Gly        | Phe        | Ser        |
| Thr Thr Pro        | Arg Phe        | Ser His<br>295 | Pro        | Val        | Ser        | Ser        | Thr<br>300 | Pro        | Ile        | Ser        | Pro        |
| Val Phe Gly<br>305 | Pro Ser        | Asn Trp<br>310 | His        | Asn        | Phe        | Val<br>315 | Pro        | Pro        | Val        | Arg        | Glu<br>320 |
| Val Val Pro        | Thr Gln<br>325 |                | Asp        | Pro        | Leu<br>330 | Leu        | Tyr        | Gly        | Ser        | Leu<br>335 | Asn        |
| Pro Val Pro        | Ile Pro<br>340 | Ala Pro        | Val        | Arg<br>345 | Lys        | Trp        | Glu        | Asp        | Val<br>350 | Val        | Ala        |
| Ala Gln Pro        |                | Leu Asp        | Thr<br>360 | Ala        | Asp        | Pro        | Ala        | Met<br>365 | Leu        | Tyr        | Ala        |
| Val Val Asp<br>370 | Gly Val        | Pro Pro<br>375 | Thr        | Arg        | Trp        | Lys        | Glu<br>380 | Phe        | Met        | Arg        | Leu        |
| Leu Gly Leu<br>385 | ı Ser Glu      | His Glu<br>390 | Ile        | Glu        | Arg        | Leu<br>395 | Glu        | Leu        | Gln        | Asn        | Gly<br>400 |
| Arg Cys Le         | ı Arg Glu      | Ala His        | Tyr        | Ser        | Met        | Leu        | Glu        | Ala        | Trp        | Arg        | Arg        |

| Arg Thr Pro Arg His Glu Ala Thr Leu Asp Val Val Gly Arg Val Leu 420 425 430   |  |  |  |  |  |  |  |  |  |  |  |  |
|---|--|--|--|--|--|--|--|--|--|--|--|--|
| Cys Asp Met Asn Leu Arg Gly Cys Leu Glu Asn Ile Arg Glu Thr Leu 435 440 445   |  |  |  |  |  |  |  |  |  |  |  |  |
| Glu Ser Pro Ala His Ser Ser Thr Thr His Leu Pro Arg 450 455 460   |  |  |  |  |  |  |  |  |  |  |  |  |
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| ccgtgatctc tatgcccgag tctcaaccct caactgtcac cccaaggcac ttgggacgtc 120   |  |  |  |  |  |  |  |  |  |  |  |  |
| cogtgatete tatgedegag teleaaceet eaactgleac eedaaggeac tigggacgte 120   |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180   |  |  |  |  |  |  |  |  |  |  |  |  |
|   |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180 katgggggag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct 233 Met Gly Leu Ser Thr Val Pro   |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180  katgggggag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct Met Gly Leu Ser Thr Val Pro  1 5  gac ctg ctg ctg cca ctg gtg ctc ctg gag ctg ttg gtg gga ata tac Asp Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr  |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180  katgggggag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct Met Gly Leu Ser Thr Val Pro 1 5  gac ctg ctg ctg cca ctg gtg ctc ctg gag ctg ttg gtg gga ata tac Asp Leu Leu Pro Leu Val Leu Leu Glu Leu Val Gly Ile Tyr 10 15 20  ccc tca ggg gtt att gga ctg gtc cct cac cta ggg gac agg gag aag Pro Ser Gly Val Ile Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys   |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180  katgggggag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct 233  Met Gly Leu Ser Thr Val Pro  1 5  gac ctg ctg ctg cca ctg gtg ctc ctg gag ctg ttg gtg gga ata tac Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr  10 15 20  ccc tca ggg gtt att gga ctg gtc cct cac cta ggg gac agg gag aag Pro Ser Gly Val Ile Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys  25 30 35  aga gat agt gtg tgt ccc caa gga aaa tat atc cac cct caa aat aat Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn   |  |  |  |  |  |  |  |  |  |  |  |  |
| ctggacagac cgagtcccgg gaagccccag cactgccgct gccacactgc cctgagccca 180  katgggggag tgagaggcca tagctgtctg gc atg ggc ctc tcc acc gtg cct 233  Met Gly Leu Ser Thr Val Pro 1 5 5 20  gac ctg ctg ctg cca ctg gtg ctc ctg gag ctg ttg gtg gga ata tac Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr 10 15 20  ccc tca ggg gtt att gga ctg gtc cct cac cta ggg gac agg gag aag Pro Ser Gly Val Ile Gly Leu Val Pro His Leu Gly Asp Arg Glu Lys 25 30 35 35  aga gat agt gtg tgt ccc caa gga aaa tat atc cac cct caa aat aat Arg Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln Asn Asn 45 50 55  tcg att tgc tgt acc aag tgc cac aaa gga acc tac ttg tac aat gac 425  Ser Ile Cys Cys Thr Lys Cys His Lys Gly Thr Tyr Leu Tyr Asn Asp |  |  |  |  |  |  |  |  |  |  |  |  |

| Ser | Phe | Thr<br>90 | Ala | Ser | Glu | Asn               | His<br>95 | Leu | Arg | His | Cys | Leu<br>100 | Ser | Cys | Ser |      |
|-----|-----|-----------|-----|-----|-----|-------------------|-----------|-----|-----|-----|-----|------------|-----|-----|-----|------|
|     |     |           |     |     |     | ggt<br>Gly<br>110 |           |     |     |     |     |            |     |     |     | 569  |
|     |     |           |     |     |     | ggc<br>Gly        |           |     |     |     |     |            |     |     |     | 617  |
|     |     |           |     |     |     | cag<br>Gln        |           |     |     |     |     |            |     |     |     | 665  |
|     |     |           |     |     |     | tgc<br>Cys        |           |     |     |     |     |            |     |     |     | 713  |
|     |     |           |     |     |     | cta<br>Leu        |           |     |     |     |     |            |     |     |     | 761  |
|     |     |           |     |     |     | gag<br>Glu<br>190 |           |     |     |     |     |            |     |     |     | 809  |
|     |     | _         | _   |     |     | gag<br>Glu        | _         |     |     |     |     |            | _   | -   |     | 857  |
|     |     |           |     |     |     | ctt<br>Leu        |           |     |     |     |     |            |     |     |     | 905  |
|     | _   |           | _   |     |     | cgg<br>Arg        |           |     |     |     |     |            |     |     |     | 953  |
|     |     |           |     |     |     | gaa<br>Glu        |           |     |     |     |     |            |     |     |     | 1001 |
|     | _   |           | _   | _   |     | aac<br>Asn<br>270 |           | _   |     | -   |     |            |     |     |     | 1049 |
|     |     |           | _   |     |     | agt<br>Ser        |           |     |     | _   |     |            |     |     |     | 1097 |
|     |     |           |     |     |     | ggt<br>Gly        |           |     |     |     |     |            |     |     |     | 1145 |
|     |     |           |     |     |     | tat<br>Tyr        |           |     |     |     |     |            |     |     |     | 1193 |

| 315   |               | 320          | 325             |             |
|---|---------------|--------------|-----------------|-------------|
| gcc ctc gcc tcc gad<br>Ala Leu Ala Ser Asp<br>330 |               |              |                 | _           |
| agc gcc cac aag ccc<br>Ser Ala His Lys Pro<br>345 |               | -            |                 | _           |
| tac gcc gtg gtg gag<br>Tyr Ala Val Val Glo<br>360 |               |              |                 |             |
| cgg cgc cta ggg cto<br>Arg Arg Leu Gly Leu<br>380 | ı Ser Asp His |              |                 |             |
| aac ggg cgc tgc ctg<br>Asn Gly Arg Cys Let<br>395 |               |              |                 |             |
| agg cgg cgc acg ccg<br>Arg Arg Arg Thr Pro<br>410 |               |              |                 |             |
| gtg ctc cgc gac atg<br>Val Leu Arg Asp Med<br>425 |               |              |                 |             |
| gcg ctt tgc ggc ccc<br>Ala Leu Cys Gly Pro<br>440 | -             | -            |                 |             |
| tgaggetgeg cecetge                                | ggg cagetetaa | g gaccgtcctg | cgagatcgcc ttcc | aacccc 1637 |
| acttttttct ggaaagga                               | agg ggtcctgca | g gggcaagcag | gagetageag eege | ctactt 1697 |
| ggtgctaacc cctcgat                                | gta catagettt | t ctcagctgcc | tgcgcgccgc cgac | agtcag 1757 |
| cgctgtgcgc gcggagag                               | gag gtgcgccgt | g ggctcaagag | cctgagtggg tggt | ttgcga 1817 |
| ggatgaggga cgctatgo                               | ect catgecegt | t ttgggtgtcc | tcaccagcaa ggct | gctcgg 1877 |
| gggcccctgg ttcgtcc                                | ctg agccttttt | c acagtgcata | agcagttttt tttg | tttttg 1937 |
| ttttgttttg ttttgtt                                | itt aaatcaatc | a tgttacacta | atagaaactt ggca | ctcctg 1997 |
| tgccctctgc ctggacaa                               | agc acatagcaa | g ctgaactgtc | ctaaggcagg ggcg | agcacg 2057 |
| gaacaatggg gccttcag                               | gct ggagctgtg | g acttttgtac | atacactaaa atto | tgaagt 2117 |
| taaaaaaaaa aaaaaaa                                | gga attc      |              |                 | 2141        |

<210> 27 <211> 455

| -212         | - DI       | am.        |            |            |            |            |            |            |            |            |            |            |            |            |            |
|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| <212<br><213 |            |            | icial      | l Sed      | quen       | ce         |            |            |            |            |            |            |            |            |            |
| <220<br><223 | > De       | escri      |            | on of      | E Art      | cific      | cial       | Sequ       | ıence      | e: hu      | uman       | TNF-       | -R ir      | า          |            |
| <400         | > 27       | 7          |            |            |            |            |            |            |            |            |            |            |            |            |            |
| Met<br>1     | Gly        | Leu        | Ser        | Thr<br>5   | Val        | Pro        | Asp        | Leu        | Leu<br>10  | Leu        | Pro        | Leu        | Val        | Leu<br>15  | Leu        |
| Glu          | Leu        | Leu        | Val<br>20  | Gly        | Ile        | Tyr        | Pro        | Ser<br>25  | Gly        | Val        | Ile        | Gly        | Leu<br>30  | Val        | Pro        |
| His          | Leu        | Gly<br>35  | Asp        | Arg        | Glu        | Lys        | Arg<br>40  | Asp        | Ser        | Val        | Cys        | Pro<br>45  | Gln        | Gly        | Lys        |
| Tyr          | Ile<br>50  | His        | Pro        | Gln        | Asn        | Asn<br>55  | Ser        | Ile        | Cys        | Cys        | Thr<br>60  | Lys        | Cys        | His        | Lys        |
| Gly<br>65    | Thr        | Tyr        | Leu        | Tyr        | Asn<br>70  | Asp        | Cys        | Pro        | Gly        | Pro<br>75  | Gly        | Gln        | Asp        | Thr        | Asp<br>80  |
| Cys          | Arg        | Glu        | Cys        | Glu<br>85  | Ser        | Gly        | Ser        | Phe        | Thr<br>90  | Ala        | Ser        | Glu        | Asn        | His<br>95  | Leu        |
| Arg          | His        | Cys        | Leu<br>100 | Ser        | Cys        | Ser        | Lys        | Cys<br>105 | Arg        | Lys        | Glu        | Met        | Gly<br>110 |            | Val        |
| Glu          | Ile        | Ser<br>115 | Ser        | Cys        | Thr        | Val        | Asp<br>120 | Arg        | Asp        | Thr        | Val        | Cys<br>125 | Gly        | Cys        | Arg        |
| Lys          | Asn<br>130 | Gln        | Tyr        | Arg        | His        | Tyr<br>135 | Trp        | Ser        | Glu        | Asn        | Leu<br>140 | Phe        | Gln        | Cys        | Phe        |
| Asn<br>145   | Cys        | Ser        | Leu        | Cys        | Leu<br>150 | Asn        | Gly        | Thr        | Val        | His<br>155 | Leu        | Ser        | Сув        | Gln        | Glu<br>160 |
| Lys          | Gln        | Asn        | Thr        | Val<br>165 | Cys        | Thr        | Cys        | His        | Ala<br>170 | Gly        | Phe        | Phe        | Leu        | Arg<br>175 | Glu        |
| Asn          | Glu        | Cys        | Val<br>180 | Ser        | Cys        | Ser        | Asn        | Cys<br>185 | Lys        | Lys        | Ser        | Leu        | Glu<br>190 | Cys        | Thr        |
| Lys          | Leu        | Cys<br>195 | Leu        | Pro        | Gln        | Ile        | Glu<br>200 | Asn        | Val        | Lys        | Gly        | Thr<br>205 | Glu        | Asp        | Ser        |
| Gly          | Thr<br>210 | Thr        | Val        | Leu        | Leu        | Pro<br>215 | Leu        | Val        | Ile        | Phe        | Phe<br>220 | Gly        | Leu        | Cys        | Leu        |
| Leu<br>225   | Ser        | Leu        | Leu        | Phe        | Ile<br>230 | Gly        | Leu        | Met        | Tyr        | Arg<br>235 | Tyr        | Gln        | Arg        | Trp        | Lys<br>240 |
| Ser          | Lys        | Leu        | Tyr        | Ser<br>245 | Ile        | Val        | Сув        | Gly        | Lys<br>250 | Ser        | Thr        | Pro        | Glu        | Lys<br>255 | Glu        |

Gly Glu Leu Glu Gly Thr Thr Lys Pro Leu Ala Pro Asn Pro Ser

| 260 | 265 | 270 |
|-----|-----|-----|
|     |     |     |

Phe Ser Pro Thr Pro Gly Phe Thr Pro Thr Leu Gly Phe Ser Pro Val 275 280 285

Pro Ser Ser Thr Phe Thr Ser Ser Ser Thr Tyr Thr Pro Gly Asp Cys 290 295 300

Pro Asn Phe Ala Ala Pro Arg Arg Glu Val Ala Pro Pro Tyr Gln Gly 305 310 315 320

Ala Asp Pro Ile Leu Ala Thr Ala Leu Ala Ser Asp Pro Ile Pro Asn 325 330 335

Pro Leu Gln Lys Trp Glu Asp Ser Ala His Lys Pro Gln Ser Leu Asp 340 345 350

Thr Asp Asp Pro Ala Thr Leu Tyr Ala Val Val Glu Asn Val Pro Pro 355 360 365

Leu Arg Trp Lys Glu Phe Val Arg Arg Leu Gly Leu Ser Asp His Glu 370 375 380

Ile Asp Arg Leu Glu Leu Gln Asn Gly Arg Cys Leu Arg Glu Ala Gln 385 390 395 400

Tyr Ser Met Leu Ala Thr Trp Arg Arg Thr Pro Arg Arg Glu Ala 405 410 415

Thr Leu Glu Leu Leu Gly Arg Val Leu Arg Asp Met Asp Leu Leu Gly 420 425 430

Cys Leu Glu Asp Ile Glu Glu Ala Leu Cys Gly Pro Ala Ala Leu Pro 435 440 445

Pro Ala Pro Ser Leu Leu Arg 450 455

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<211> 13

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<220>

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 amino acid sequence of protein purified from urine
 (main sequence)

<220>

<221> UNSURE

<222> (4)

<223> identity of "Xaa" could not be determined

<400> 28

Asp Ser Val Xaa Pro Gln Gly Lys Tyr Ile His Pro Gln 1 5 10

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<210> 29
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      (subsidiary sequence)
<220>
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<222> (7)
<223> identity of "Xaa" could not be determined
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 1
<210> 30
<211> 151
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<213> Homo sapiens
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caggggaaaa tattcaccct caaataattc gatttgctgt accaagtgcc acaaaggaaa 60
ctacttgtac aatgactgtc caggcccggg gcaggatacg gactgcaggg agtgtgagag 120
                                                                   151
cggctccttc acagcctcag aaaacaacaa g
<210> 31
<211> 8
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      cleavage peptide
<400> 31
Asp Ser Val Cys Pro Gln Gly Lys
 1
<210> 32
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<212> PRT
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      cleavage peptide
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<222> (1)..(2)
<223> identity of "Xaa" could not be determined
Xaa Xaa Leu Ser Cys Ser Lys
<210> 33
<211> 7
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     cleavage peptide
<400> 33
Asp Thr Val Cys Gly Cys Arg
<210> 34
<211> 11
<212> PRT
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     cleavage peptide
Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys
                5
<210> 35
<211> 12
<212> PRT
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     cleavage peptide
<400> 35
Glu Asn Glu Cys Val Ser Cys Ser Asn Cys Lys
<210> 36
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<220>
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<222> (6)
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<210> 37
<211> 14
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<213> Artificial Sequence
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      cleavage peptide
<400> 37
Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu Asn Asn Lys
                  5
<210> 38
<211> 8
<212> PRT
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      cleavage peptide
<400> 38
Leu Val Pro His Leu Gly Asp Arg
<210> 39
<211> 15
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      cleavage peptide
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<400> 39
Lys Glu Met Gly Gln Val Glu Ile Ser Ser Cys Thr Val Asp Arg
                  5
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<210> 40
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                  5
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<210> 42
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                  5
                                      10
                                                          15
 1
Thr Val Cys Gly
             20
<210> 43
<211> 19
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<212> PRT
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<222> (6)
<223> indentity of "Xaa" could not be determined
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<221> UNSURE
<222> (18)
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Gly Xaa Tyr
<210> 44
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                                      10
Xaa Arg
<210> 45
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      cleavage peptide
<400> 45
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Leu Cys Leu Pro Gln Ile Glu Asn
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  1
<210> 46
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                                     1.0
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Asp Ser Val Cys Pro Gln Gly Lys Tyr Ile His Pro Gln
                 5
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<212> PRT
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                  5
<210> 50
<211> 20
<212> DNA
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<223> Description of Artificial Sequence: hybridization
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<400> 50
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caaggtaaat atattcatcc
<210> 51
<211> 20
<212> DNA
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      probe
<400> 51
                                                                    20
cagggtaagt acatccatcc
<210> 52
<211> 20
<212> DNA
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      probe
<400> 52
                                                                    20
caaggtaaat atatacatcc
<210> 53
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<212> DNA
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      probe
<400> 53
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| caaggcaaat atattcatcc   | 20 |
|---|----|
| <210> 54<br><211> 20<br><212> DNA<br><213> Artificial Sequence      |    |
| <220> <223> Description of Artificial Sequence: hybridization probe |    |
| <400> 54 cagggcaagt acatccaccc                                      | 20 |
| <210> 55<br><211> 20<br><212> DNA<br><213> Artificial Sequence      |    |
| <220> <223> Description of Artificial Sequence: hybridization probe |    |
| <400> 55 caaggcaaat atatacatcc                                      | 20 |
| <210> 56<br><211> 20<br><212> DNA<br><213> Artificial Sequence      |    |
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| <400> 56 caaggaaaat atattcatcc                                      | 20 |
| <210> 57<br><211> 20<br><212> DNA<br><213> Artificial Sequence      |    |
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| <400> 57 cagggaaagt acatccaccc                                      | 20 |
| <210> 58  |    |

| <212><br><213>            | > DNA<br>> Artificial Sequence   |    |
|---------------------------|--|----|
| <220><br><223>            | <pre>&gt; &gt; Description of Artificial Sequence: hybridization     probe</pre> | on |
| <400><br>caagga           | > 58<br>gaaaat atatacatcc  | 20 |
| <210><211><211><212><213> | > 20   |    |
| <220><br><223>            | <pre>&gt; &gt; Description of Artificial Sequence: hybridization     probe</pre> | on |
| <400><br>caaggg           | > 59<br>ggaaat atattcatcc  | 20 |
| <210><211><212><213>      | > 20   |    |
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| <400><br>cagggg           | > 60<br>ggaagt acatccaccc  | 20 |
| <210><211><212><213>      | > 20   |    |
| <220><br><223>            | > > Description of Artificial Sequence: hybridization probe                      | on |
| <400><br>caaggg           | > 61<br>ggaaat atatacatcc  | 20 |
| <210><211><211><212><213> | > 14   |    |
| <220><br><223>            | > > Description of Artificial Sequence: TNF-BP trypt                             | ic |

## cleavage peptide

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<400> 62
Glu Cys Gly Ser Gly Ser Phe Thr Ala Ser Glu Asn Asn Lys
<210> 63
<211> 14
<212> PRT
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<223> Description of Artificial Sequence: TNF-BP tryptic
      cleavage peptide
<400> 63
Glu Cys Gly Ser Gly Ser Phe Thr Ala Ser Cys Asn Asn Lys
<210> 64
<211> 8
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      cleavage peptide
<400> 64
Phe Thr Ala Ser Glu Asn Asn Lys
<210> 65
<211> 8
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      cleavage peptide
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                 5
<210> 66
<211> 30
<212> DNA
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<223> Description of Artificial Sequence: hybridization
      probe
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| <400> 66 aaatgacgga gactcttgtt gttcctaggg                           | 30 |
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| <210> 67<br><211> 30<br><212> DNA<br><213> Artificial Sequence      |    |
| <220> <223> Description of Artificial Sequence: hybridization probe |    |
| <400> 67 aagtggcgta gtcttttgtt gttcctaggg                           | 30 |
| <210> 68 <211> 30 <212> DNA <213> Artificial Sequence               |    |
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| tcg cac aaa gga acc tac ttg tac aat gac tgt cca ggc ccg ggg cag<br>Ser His Lys Gly Thr Tyr Leu Tyr Asn Asp Cys Pro Gly Pro Gly Gln<br>20 25 30             | 96  |
| gat acg gac tgc agg gag tgt gag agc ggc tcc ttc aca gcc tca gaa<br>Asp Thr Asp Cys Arg Glu Cys Glu Ser Gly Ser Phe Thr Ala Ser Glu<br>35 40 45             | 144 |
| aac aac aag gatcc  | 158 |

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| ttg            |  | 63        |
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| \Z1J/          | Artificial Sequence  |           |
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| <211><br><212><br><213>      |   |    |
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| <210><211><211><212><212>    | 81  |    |
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| ccatgg                       | gcct ctccaccgtg c   | 81 |
| <210><211><212><212><213>    | 17  |    |
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| <210><211><211><212> <213> < | 17  |    |
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| <211> 1  |   |   |
| <212> D  |   |   |
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| u  | niversal primer   |   |
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|  | ccag tcacgac 1  | 7 |
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| <pre>gttttcc &lt;210&gt; 9 &lt;211&gt; 1 &lt;212&gt; D &lt;213&gt; A &lt;220&gt; &lt;223&gt; D E &lt;400&gt; 9</pre> | ccag tcacgac 1  27 .8 20 20 21 21 22 22 23 25 26 27 27  | 7 |